OBSERVATIONS ON THE PATHOGENESIS OF GASTRIC ULCER

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THE inescapable equation of ulcer ætiology—acid-pepsin aggression versus mucosal defence—allows for certain differences in the pathogenesis of duodenal and gastric ulcer. In duodenal-ulcer patients, gastric secretion is characteristically higher, the acid-bearing (fundic) area of the stomach larger, the gastric mucosa thicker (figs. 1 and 2), and the parietal-cell mass greater than is usual in normal people (Cox 1952, Card and Marks 1959). Gastric-ulcer patients, on the other hand, often have normal or subnormal secretion and atrophic mucosal changes (figs. 3 and 4). It is thus understandable that an increase in acid and pepsin should be incriminated as the dominant ætiological factor in duodenal ulcer, and impaired mucosal resistance as the underlying cause of gastric ulcer (Illingworth 1956). Differences in gastric motor activity in patients with gastric ulcer and in those with duodenal ulcer have been interpreted as further evidence in favour of different ætiologies. The overlap in gastric secretory response (Ivy et al. 1950, Grossman 1951) and parietal-cell mass (Cox 1952) between duodenal-ulcer patients and normal subjects, however, is so great that the differences cannot account for all duodenal ulcers. Moreover, in the large majority of patients with healed gastric ulcer the secretory response, when tested by fractional gastric analysis, is greater than the average normal—a finding which suggests a fundamental similarity between gastric and duodenal ulcers (Hurst and Venables 1929). The observed difference in motor and secretory function may be an effect of the ulcerative process on the mucosa, rather than the result of a difference in ætiology (Shay et al. 1942, Hollander 1947, Shay and Lorber 1951). In the present paper we shall consider the pathogenesis of gastric ulcer against a background of the situation of the ulcer in the stomach, the histological appearance of the gastric mucosa, and the associated secretory patterns.

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Observations

Situation of the Ulcer

Examination of surgical and necropsy material shows that only few gastric ulcers are situated in the acid-bearing area of the stomach. Stout (1947) found 93% of 113 gastric ulcers and Karsner (1949) 94% in the pyloric area, where acid is not secreted. This is often overlooked because of a tendency to consider the histology of the stomach in terms of its gross anatomical rather than histological subdivisions (Grossman 1958). Landboe-

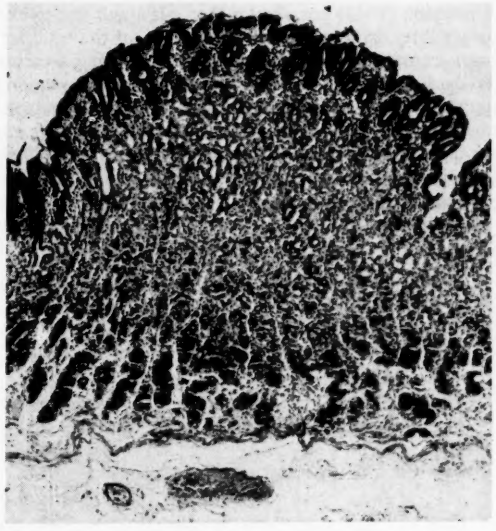

Fig. 2—Photomicrograph of the mucosa shown in fig. 1: normal glandular architecture and only minimal gastritis (×50).

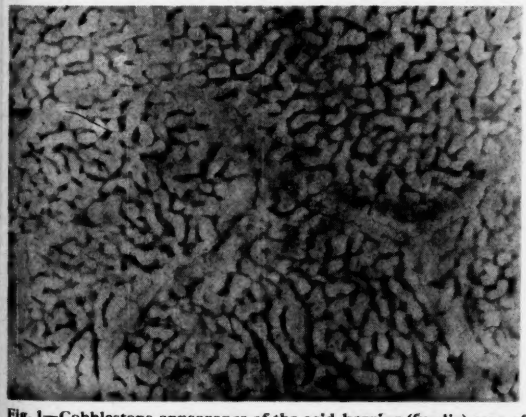

Fig. 1—Cobblestone appearance of the acid-bearing (fundic) area of the stomach in a duodenal-ulcer subject with a maximum acid output of 80 mEq. HCl per hour.

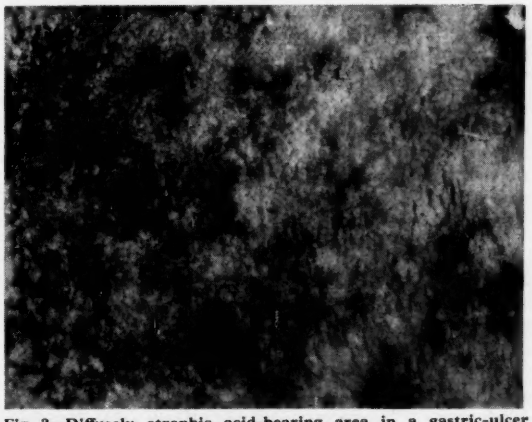

Fig. 3—Diffusely atrophic acid-bearing area in a gastric-ulcer subject with a maximum acid output of 1 mEq. HCl per hour. A submucosal vein is visible through the thin mucosa.

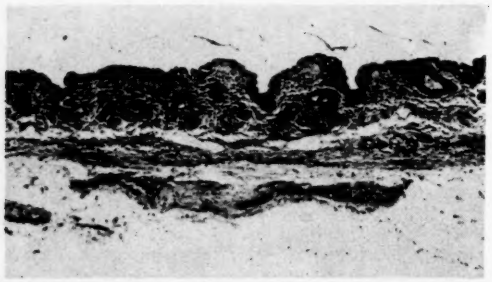

Fig. 4—Photomicrograph of mucosa shown in fig. 3: gross destruction of glandular architecture and diffuse cellular infiltration (×50).

Christensen (1944) has shown that, although the pyloric mucosa lines on the average only 11·5% of the total area of the stomach, it covers 43·7% of the lesser curvature. His data indicate that the pyloric mucosa commonly extends above the incisura angularis, a variable landmark erroneously regarded by many clinicians, anatomists, and even histologists as the junction between the " body " and " pyloric " portions of the stomach (figs. 5A and B).

The gastric ulcer shown in figs. 6–8 was thus thought to be in the body and, by inference, in the acid-bearing area. Histologically, however, the lesion was in the pyloric gland area just distal to its junction with the acid-bearing area.

Gastric ulcers are commonly found in this region (Holmes and Hampton 1933, Ihre and Muller 1943, Ivy et al. 1950, Miura 1958). In our series 13 were distal and 20 proximal to

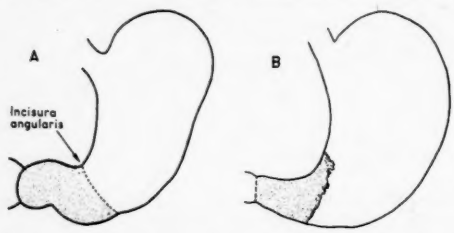

Fig. 5—Diagrammatic representation of pyloric portion of stomach (pyloric gland area) modified after Goss (1954) in A and after Landboe-Christensen (1944) in B. The pyloric portion is shaded.

the incisura angularis. 18 of the latter groups extended to within 2·5 cm. of the incisura; and all these were within the distal 44% of the lesser, or posterior lesser, curvature of the stomach. Only 2 were clearly in the acid-bearing area (table I). Our series showed a sex difference in the location of gastric ulcer similar to that described by Ivy et al. (1950).

These data are consistent with the finding that the pyloric-gland area is the site of predilection of gastric ulcers (Stout 1947, Karsner 1949), and with our belief that these lesions are often on the lesser, or posterior lesser, curvature just distal to the junction of the acid-bearing and pyloric-gland areas.

Histology of the Gastric Mucosa

Patients with gastric ulcer invariably have chronic and atrophic pyloric gastritis (Magnus 1952), and this is sometimes most noticeable in the proximal portion of the pyloric-gland area (Card and Marks 1959). The degree of gastritis in the acid-bearing area varies considerably.

A few have diffuse chronic gastritis, atrophic gastritis, or both; and in them the gastric ulcer is usually within the acid-bearing area. In others—particularly those with prepyloric ulcers—the acid-bearing mucosa is indistinguishable from the normal or even from that of duodenal-ulcer patients.

Card and Sircus (1958) have noted that a centrifugally distributed " zonal gastritis " around gastric ulcers often involves the acid-bearing area; it consists of a central zone of atrophy surrounding the ulcer, with superficial and chronic gastritis more peripherally.

These findings strongly suggest that in some patients a spreading atrophic gastritis in the acid-bearing area may be a sequel to gastric ulceration. Despite the lack of conclusive evidence on the role of chronic or atrophic gastritis in the localisation of gastric ulcers, it is probable that the diminished mucosal resistance associated with such gastritis does in fact predispose to ulceration. If so

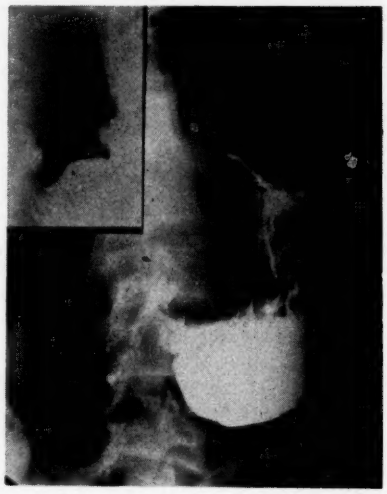

Fig. 6—Gastric ulcer situated above the level of the incisura angularis.

gastritis may be both a predisposing cause of, and a sequel to, ulceration.

Secretory Patterns

Gastric ulceration is said to be associated with normal or low acid secretion, especially as measured by the Ewald test-meal. The acid output after maximal histamine stimulation varies from virtual achlorhydria in some gastric-ulcer patients to levels well within the duodenal-ulcer range in others; its mean value has been reported as slightly above normal in a group of 20 men (Kay 1953) but significantly lower than normal in a smaller series of men and women (Marks 1957). We investigated our 33

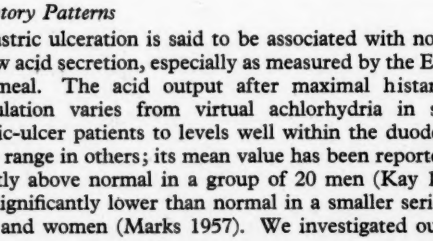

Fig. 7—The mucosal surface of resected portion of stomach shown in fig. 6. The gastric ulcer is situated within the pale pyloric-gland area.

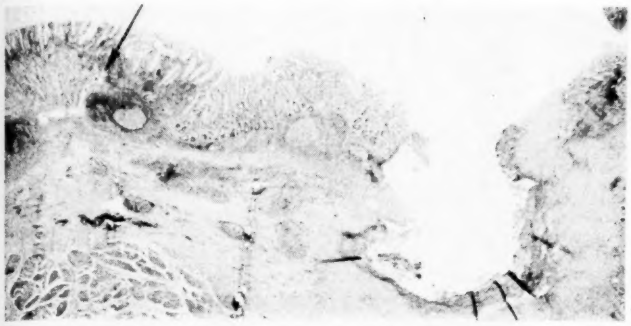

Fig. 8—Photomicrograph of the same gastric ulcer. It is situated just distal to the junction between the pyloric area and the acid-bearing area of the stomach. The arrow points to the junction of the two types of mucosa (×9).

patients to assess the effect of the situation of the lesion and of the duration of symptoms on the " maximum acid output " (M.A.O.) and the maximum histamine response (M.H.R.).†

The ulcers were divided into the three groups, as suggested by Johnson (1957a)—prepyloric ulcers (type III), gastric ulcers associated with duodenal ulcers or scarring (type II), and all other gastric ulcers (type I) (tables I and II). The M.H.R. was determined as described by Kay (1953) and the M.A.O. by a slight modification of his augmented histamine test (Card and Marks 1959). The mean value for the series was somewhat lower than the mean value in hospital controls. The values in the prepyloric-ulcer group were similar to, or higher than, in the controls. The mean M.A.O. in patients with gastric ulcer associated with duodenal ulcer or scarring was slightly greater than that in hospital controls and lower than in patients with uncomplicated duodenal ulcer. In the third group the M.A.O. ranged from virtual achlorhydria to 19·1 mEq. HCl per hour. In the great majority of patients in this group the gastric ulcer was situated in the vicinity of the incisura; and, in contrast to the first two groups, the duration of symptoms was related to the M.A.O. Patients with many years' history often had a low output, and those with a short history a high output. The secretory findings in the three groups might have been anticipated in view of the highly significant correlation between the acid output and the parietal-cell mass (Marks 1956, Marks et al. 1958) and the reduced parietal-cell mass in patients with chronic and atrophic gastritis of the acid-bearing area (Cox 1952).

These observations are compatible with the histological findings in the acid-bearing area in the various groups; and they support the hypothesis that gastritis associated with a reduction in the secretory response may be a consequence of gastric ulcer. This reduction in secretion is not necessarily irreversible.

Hurst and Venables (1929) used fractional gastric analysis and Watkinson (1951) twenty-four-hour test-meals to show that gastric secretion may increase appreciably after the healing of a gastric ulcer. The results of repeat augmented-histamine tests in two of our patients (cases 10 and 19) support this finding. It may be inferred that at least one reason for the altered secretory response in these patients is the increase in the number of functioning parietal cells after healing of the ulcer. We do not know whether this is due to the regeneration or to functional recovery; but the latter possibility appears the more likely, since mitoses are extremely rare in parietal cells (Palmer 1951, 1954, Card and Marks 1959, Popoff 1941).

† The " maximum acid output " (M.A.O.) is defined as the acid output during the first hour following the subcutaneous injection of 0·04 mg. histamine acid phosphate per kg. body-weight. The acid output during the half-hour period from fifteen to forty-five minutes after the administration of histamine is the " maximum histamine response " (M.H.R.).

Discussion

Hurst and Stewart (1929) observed duodenal ulceration or scarring in 12% and Wilkie (1926) in 53% of gastric-ulcer patients. 10 of our 33 gastric-ulcer patients had a coincident duodenal ulcer or scar (table I). The development of a duodenal ulcer after healing of a gastric ulcer (Watkinson 1951) must be very unusual: both Tanner (1954) and Johnson (1957b) have noted that the duodenal lesion always develops first. Tanner (1954) found that the gastric ulcer was active and the duodenal ulcer inactive or healed in 90% of these patients; whereas in association with an active duodenal ulcer the gastric ulcer often appeared to be an early or subacute lesion.

Johnson (1957a) and Dragstedt (1958) attribute the gastric ulcer to diminished gastric motility or to the development of pyloric stenosis and gastric retention. Stenosis or retention, however, are not invariable; and it has not yet been ascertained whether the diminished motility in patients without stenosis precedes or follows the gastric ulceration. Tanner (1954) believes that in patients with duodenal ulcer the onset of gastritis and the development of atrophic mucosal changes causes a reduction in hypersecretion and healing of the ulcer; but the

TABLE I—DATA ON 33 CONSECUTIVE PATIENTS WITH GASTRIC ULCER

No.	Age and sex	Site of ulcer *	Duration of dyspepsia (years)	M.H.R. (mEq. HCl per 30 min.) Free acid	M.H.R. (mEq. HCl per 30 min.) Total acid	M.A.O. (mEq. per hour) total acid
Gastric ulcer (type I):						
1	50 F	I	3 months	10·3	10·9	19·1
2	56 F	B	4 months	8·1	9·0	16·3
3	50 F	I	6 months	3·6	4·1	5·6
4	29 M	I+	6 months	1·8	2·3	4·1
5	47 F	I+	6 months	0·6	1·2	2·8
6	51 M	I+	1	14·0	16·0	25·3
7	43 F	I	1	9·0	10·0	17·0
8	31 F	I	1	7·7	8·3	15·0
9	51 F	I	1	3·7	4·8	8·3
10	70 M	I	4	2·9	4·1	6·6†
11	60 M	I	5	4·2	4·9	8·1
12	75 M	I+	11	1·2	1·9	3·0
13	49 F	B+	12	0·6	1·2	1·7
			Mean	5·2	6·1	10·2
Gastric ulcer associated with duodenal ulcer or scarring (type II):						
14	46 M	I, DU+	1½	14·7	16·4	29·1
15	82 F	P, DS	2	6·8	7·5	13·0
16	40 F	I, DS	3	24·3	26·3	43·8
17	54 F	I, DS	4	7·2	8·0	15·7
18	56 M	P, DS+	5	11·6	12·7	22·4
19	41 M	I, DS	10	15·6	16·6	27·6‡
20	68 M	P, DS+	12	13·2	14·1	23·6
21	49 F	I, DS	15	14·9	16·0	27·8
22	49 M	I, DS	18	15·3	17·0	27·6
23	48 M	I, DS+	20	7·3	8·5	10·8
			Mean	13·1	14·3	24·1
Prepyloric ulcers (type III):						
24	34 M	PC+	2 months	22·9	24·6	44·5
25	66 M	PC+	3 months	18·5	19·0	32·7
26	56 M	P	6 months	10·1	10·9	17·3
27	68 M	P	1	21·3	23·5	42·1
28	39 M	PC+	1½	12·1	13·2	24·2
29	51 F	P	1½	6·6	7·0	12·0
30	82 M	P+	3	11·9	13·7	26·6
31	39 M	P+	4	9·5	10·6	18·0
32	50 M	PC+	15	6·3	7·4	11·6
33	63 M	P	20	11·1	13·2	21·5
			Mean	13·0	14·3	25·1

* PC = pyloric canal, just proximal to duodenal bulb.
P = pyloric-gland area distal to incisura angularis.
I = lesser or posterior lesser curvature, at or just proximal (<2·5 cm.) to the incisura angularis.
B = remainder of stomach.
DU = duodenal ulcer.
DS = duodenal scar.
\+ = Site of ulcer confirmed by surgery.

† The M.A.O. was 11·6 mEq. HCl per hour when the patient was tested during a remission 1 year later.

‡ The M.A.O. was 42·6 mEq. HCl per hour when the patient was tested during a remission five months later.

TABLE II—THE MEAN "MAXIMUM HISTAMINE RESPONSE" AND "MAXIMUM ACID OUTPUT" IN GASTRIC-ULCER PATIENTS, HOSPITAL CONTROLS, AND DUODENAL-ULCER PATIENTS

Clinical material	M.H.R. (mEq. HCl per 30 min.)		M.A.O. (mEq. HCl per hour) total acid
	Free acid	Total acid	
Gastric ulcer (male and female), 33 patients (present study)	10·0 ± 1·1	11·1 ± 1·2	18·9 ± 2·0
Gastric ulcer (male), 20 patients (Kay 1953)	13·1	..	..
Hospital controls (male), 25 patients (Kay 1953)	11·6	..	..
Hospital controls (male), 31 patients (Marks and Shay 1959)	12·2 ± 1·2	13·4 ± 1·3	23·2 ± 2·4
Hospital controls (female) 10 patients (Murray et al. 1957)	..	9·9 ± 1·2	..
Hospital controls (female), 15 patients (Marks and Shay 1959)	8·1 ± 1·1	8·9 ± 1·2	15·0 ± 1·2
Duodenal ulcer (male), 103 patients (Kay 1953)	22·9	..	..
Duodenal ulcer (male and female), 63 patients (Marks and Shay 1959)	20·2 ± 1·0	22·0 ± 1·0	38·1 ± 1·9

gastritis depresses gastric mucosal resistance and this predisposes to gastric ulceration. Our interpretation, except for a slight modification, is essentially in agreement with this view. Chronic and even atrophic pyloric gastritis affects, to a greater or lesser extent, all patients with duodenal ulcer (Magnus 1952); and the thick glandular mucosa of the acid-bearing area often presents a striking contrast to the atrophic pyloric-gland area. The atrophic changes are sometimes most pronounced along the lesser curvature just distal to the acid-bearing area; and gastric ulcers, especially those associated with duodenal ulcer or scarring, are often found in this junctional zone. The zone of gastritis surrounding a gastric ulcer usually encroaches on the acid-bearing area and leads to functional impairment or destruction of parietal and peptic cells. This is reflected in the diminished M.A.O. Since the initial involvement of the acid-bearing area may be slight, the high acid output of patients with duodenal ulcer need not be much reduced.

The interval between the onset of duodenal and gastric ulcers may reflect the inherently greater mucosal resistance of the stomach; and the acid-pepsin factor may be equally important in the ætiology of both lesions. The pyloric-gland area has a lower resistance than the acid-bearing area (Illingworth 1956), and it is interesting to speculate whether chronic exposure to acid and pepsin may lead to both gastritis and subsequent ulceration in this part of the stomach.

Conclusions

Duodenal ulceration, in common with all other types of peptic ulcer, may occur either in normal mucosa exposed to abnormally high acid-pepsin secretion or in mucosa abnormally susceptible to injury even by diminished acid-pepsin secretion. In patients with the combined lesions, gastric ulceration does not start before duodenal ulceration, because the mucosal defences of the stomach are normally greater than in the duodenum.

Longstanding hypersecretion may be an ætiological factor in chronic pyloric gastritis. Often this is most noticeable in the region adjacent to the acid-bearing area. Mucosal resistance may then diminish, and a gastric ulcer may follow.

The gastric ulcer may initiate a spreading gastritis of the acid-bearing mucosa. This would lead to functional impairment and destruction of peptic and parietal cells, with consequent diminution of the secretory response.

This sequence suggests a fundamental ætiological similarity between gastric and duodenal ulcers when they occur in the same patient. It is probable that in their pathogenesis prepyloric and other gastric ulcers do not differ from gastric ulcers associated with duodenal ulcer: the same conflict of acid-pepsin aggression versus mucosal defence applies to all. This explains the frequent location of gastric ulcers in the pyloric-gland area where resistance is lower and exposure to mechanical trauma greater than in the acid-bearing area.

The pyloric-gland area becomes particularly vulnerable with the development of pyloric stenosis when gastric stasis leads to increased release of gastrin (Dragstedt 1958). It may be justifiable to regard most gastric ulcers as "junctional ulcers", since they are found most commonly just distal to the junction of the acid-bearing and the pyloric-gland areas.

Summary

The junction of the pyloric mucosa and the acid-bearing mucosa of the stomach commonly extends above the level of the incisura. The pyloric mucosa is the site of predilection of gastric ulcers; and the vast majority of such ulcers are situated in the vicinity of the incisura angularis.

The histological and secretory pattern of three types of gastric ulcers—prepyloric ulcers, gastric ulcers associated with duodenal ulcers, and other gastric ulcers—reflect differences in their situation in the stomach.

Around gastric ulcers a centrifugally distributed zonal gastritis may involve the acid-bearing area. This may depress the secretion of acid.

Our observations suggest an ætiological similarity between gastric ulcers and duodenal ulcers.

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Addendum

Since this paper was submitted, publications by Mangold (1958) and Oi et al. (1959) have appeared which

present data pertinent to our report. Mangold (1958) surveyed a series of 157 patients with combined gastric and duodenal ulcer; X-ray evidence of delayed gastric emptying was noted in 19%, but only 9% had organic pyloric stenosis. Gastric ulceration apparently preceded the development of duodenal ulceration in 6% of his patients. Oi et al. (1959) examined the stomach histologically in 185 gastric-ulcer patients. The junction between the acid-bearing (fundic) and pyloric-gland areas varied from 2 to 16 cm. from the pyloric ring, and the gastric ulcers were invariably located within the pyloric-gland area; the vast majority were situated just distal to the junction between the latter and the acid-bearing area.

DUODENAL AND GASTRIC ULCER IN THE SAME PATIENT

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OF 313 patients with gastric ulcer, treated between 1944 and 1955, the gastric ulcer was associated with duodenal ulceration in 120. Of 100 duodenal-ulcer patients only 2 showed evidence of past gastric ulcers (table I).

Relatively few reports on patients with coexistent duodenal and gastric ulcers have been published.

Among 779 cases of benign gastric ulcer Comfort et al. (1957) found 184 which were associated with duodenal ulcer. The sex and age distribution of the patients and the size and site of the gastric ulcers were essentially the same in the two groups; but multiple gastric ulcers were twice as common in the patients who also had duodenal ulcer.

During a five-year period Walters (1957) observed 73 patients with combined gastric and duodenal ulcer. After partial gastrectomy—with gastrojejunostomy in 54 and gastroduodenostomy in 19—none developed recurrent ulcers. Nor did Hickinbotham (1956) find any recurrent ulcers after resection in 19 patients with duodenal plus gastric ulcer.

The condition was considered in detail by Johnson (1956) who had collected 135 patients with associated gastric and duodenal ulcers. A duodenal ulcer had previously been diagnosed in 70, while a gastric ulcer was followed by a duodenal ulcer in only 7. The commonest operative finding was the healed scar of a duodenal ulcer, usually associated with an active, often huge, and sometimes bleeding gastric ulcer. In 64% of cases, the combined ulceration could be explained by gastric retention which was demonstrated either radiographically, clinically, or at operation. Johnson recommends that such cases should be treated as duodenal ulcers with an extensive resection, since hypersecretion is often a prominent feature.

TABLE I—ANALYSIS OF 313 GASTRIC ULCERS

Type of ulcer	Numbers
Primary gastric ulcer	155
Gastric and duodenal ulcers	120
Pyloric ulcer	20
Doubtful *	18
Total	313

* Cases of gastric ulcers which may have been preceded by duodenal ulceration but in which evidence was inconclusive.

TABLE II—ORDER OF APPEARANCE OF THE DOUBLE LESIONS

Groups	Sequence of events	Number of cases
First group	Duodenal ulcer→healed scar of duodenal ulcer + gastric ulcer	24
	Duodenal ulcer→duodenal ulcer + gastric ulcer	6
	Duodenal ulcer→gastric ulcer	41
	Healed scar of duodenal ulcer + gastric ulcer	23
Second group	Duodenal ulcer + gastric ulcer	8
Third group	Gastric ulcer→duodenal ulcer	18
	Total	127

In an earlier study Johnson (1955) found that the incidence of associated gastric and duodenal ulcer was 9% in a series of surgically treated peptic-ulcer patients, and that gastric ulcer was preceded by a duodenal ulcer in 66% and followed by a duodenal ulcer in 5%.

The Present Series

Duodenal and gastric ulcers occurred in the same patient in 120 cases in our series. These could be divided into three groups (table II).

The First Group

In 94 patients the duodenal ulcer was followed by gastric ulceration.

On admission 24 showed signs of a healed duodenal lesion; 6 had concomitant active duodenal and gastric ulcers; and 41 showed only gastric ulceration. A feature common to all 94 was that X-ray examination had previously revealed a duodenal ulcer. In each of the first two subgroups there was 1 patient with a healed gastric ulcer; the others had active ulcers.

On admission the diagnosis was made in 86 cases at operation and in the remaining 6 by X-ray examination.* A crater in the duodenal bulb was interpreted as an active duodenal ulcer and a deformed shrunken duodenal bulb without a crater as a healed ulcer.

The Second Group

In 8 patients examination on admission revealed activity in both duodenal and gastric ulcers. But, as earlier radiographs were not available, we could not decide which of the two lesions came first, or if they had developed simultaneously. We made the diagnosis at operation in 5 and by radiography in the remaining 3 cases.

The Third Group

In 18 patients gastric ulceration preceded the duodenal ulcer.

In this group the diagnosis on admission was made at operation in 17 cases and by X-ray examination in 1 case. We were impressed by the fact that 10 patients who had previously had a perforated ulcer (all operated on and sutured) showed radiographic signs of duodenal ulcer. The perforation had been situated in the prepyloric region in 8, including 5 in which radiography later revealed a deformed duodenal bulb without an ulcer crater. It is possible that a perforation in the prepyloric region may result in adhesions to the surrounding structures: these might give rise, without any actual duodenal ulceration, to the X-ray appearance of a deformed duodenal bulb without a crater. If this assumption be correct, these 5 cases should not be included in this group. In 3 cases in which a prepyloric perforation was followed by radiographic demonstration of a crater in the duodenal bulb, and in 2 cases in which the perforation was in the middle of the lesser curvature, the duodenal ulcer must have followed the gastric lesion.

* The films of all cases in which the diagnosis rested on radiographic evidence alone were reviewed by Prof. Gregers Thomsen, M.D., of the department of radiology, Rigshospitalet, Copenhagen. We are greatly indebted to him for his help.

Discussion

Many cases included in this series were recognised only after close review and reappraisal of the case-records, while others had to be excluded because their operation notes gave no definite information of dual ulceration. We think it likely that histological examination of the duodenal segment removed at resection for gastric ulcer would reveal the remains of a previous duodenal ulcer far more often than our series would suggest. That our figure of 30% should be considered as a minimum is supported by the observation that many gastric-ulcer patients suffer from dyspepsia for long periods before X-ray examination reveals the ulcer in the stomach. These patients may have had a duodenal ulcer which has healed without leaving any scar.

On the evidence of this series we cannot decide whether most gastric ulcers are preceded by a duodenal ulcer or whether there are two types of gastric ulcers—one which follows duodenal ulceration and one which is a primary lesion. A close analysis of the history, symptoms, signs, and complications of future cases may favour one of these possibilities.

A gastric ulcer following a duodenal ulcer can be explained in two different ways.

1. The disease may have begun as an active ulcer with hypersecretion of acid, which is gradually superseded by normal or diminished secretion. Most patients in our series were given an Ewald test-meal before operation; and we compared the results with those of previous test-meals. The acid secretion had diminished in only 14 patients: in the others it had either remained constant or increased. This cannot be taken as decisive evidence, however: most authorities regard test-meals as unreliable.

2. The disease may have begun with a duodenal ulcer, which results in an organic or spastic pyloric stenosis and the development of an ulcer proximal to the stenosis. This second hypothesis agrees with the observations of Johnson, who found signs of gastric retention in many cases of concomitant duodenal and gastric ulcer. 81 patients in our first group were studied by means of Kemp's retention test-meal (those with perforation were not subjected to this test): gastric retention was noted in 13, while 68 showed no retention after six hours. Among the 86 patients who were subjected to operation, 10 showed evidence of pyloric stenosis; and among the 8 patients who were not operated on 1 had radiographic signs.

Thus, many of our patients had no signs of gastric retention during the hospital stay. If pyloric stenosis was the cause of their gastric ulcer it must have been spastic in nature and it must have occurred earlier in the course of the disease.

Summary

The case-histories of 313 patients with gastric ulcer were analysed. In 30% the disease began with a duodenal ulcer. In only 6% was a gastric ulcer followed by a duodenal ulcer.

The case-histories of 100 patients with duodenal ulcer showed that in only 2% had this condition been preceded by a gastric ulcer.

Secondary gastric ulceration can be interpreted in two different ways; and further studies are needed to elucidate its pathogenesis.

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MECHANISM OF ARTERIAL SPASM FOLLOWING INTRA-ARTERIAL INJECTION OF THIOPENTONE

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ALTHOUGH thiopentone ('Pentothal Sodium') is constantly given by intravenous injection without mishap, there are a few records of accidents when by chance the injection has been made into an artery. In 1943 Macintosh and Heyworth described two cases in which it had been injected in this way.

In one of these 1·5 ml. of a 10% solution had been given, and one hour later the patient complained of pain in the hand on the side of the injection. The hand and the distal part of the forearm were blanched and the radial artery was not palpable. After an eight-day interval the patient again had severe pain in his hand, which was found to be ischæmic and cold. The pulsation was strong in the brachial artery but there was no radial pulse. Two days later pieces of the brachial and of the radial arteries were resected, and the radial artery was found completely thrombosed.

Other cases have been described by Lundy (1942) who used a 2·5% solution in two cases; the injection was stopped because the patient complained of a burning sensation in his hand, and the needle was found to be in an artery. Cohen (1948) described a further eight cases. In some of these, massive gangrene of the limb followed extensive thrombosis in major vessels.

The observations which we have made were undertaken because Sir Robert Macintosh wished to know whether there was any pharmacological evidence which threw light on the effect of thiopentone given intra-arterially. This request came at a time when we had been obtaining evidence of new factors concerning arterial tone, and we had studied various substances which appeared to act by liberating noradrenaline from structures in or near the artery wall (Burn and Rand 1958a). It seemed worth while to examine thiopentone to see if it, too, had the type of action mentioned.

Methods

Observations were first made on spiral strips of rabbit aorta removed from the thorax of the freshly killed rabbit and suspended in an isolated organ bath so that contractions could be recorded. The principal experiments, however, were carried out by perfusing the ears of rabbits. The central artery running along the dorsum of the ear was cannulated near the base of the ear, and Locke's solution from a Marriotte bottle was then perfused. The venous effluent from the open ends of the veins was collected in a funnel and passed into an outflow recorder of the pattern devised by Stephenson (1948). The outflow was recorded on a kymograph.

Three experiments were made in which the hindleg of a dog was perfused with blood from a Dale-Schuster (1928) pump, and two experiments were made in which a cat's tail was perfused with Locke's solution containing 4% sucrose.

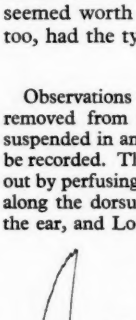

Fig. 1—Records of contractions produced in a spiral strip of rabbit aorta which was suspended in a bath of 8 ml. capacity.
The addition to the bath of 5 mg. thiopentone (P) caused the first contraction. The bath fluid was changed after 1·5 min., and the aorta then relaxed. The addition of 2 mg. thiopentone then caused a smaller contraction.

Results

Rabbit Aorta Strips

The experiments on spiral strips of rabbit aorta showed that thiopentone always caused contraction of the smooth muscle of the artery wall. Since we were accustomed to the observation that the intravenous injection of thiopentone causes a fall of blood-pressure, we did not expect this result; but it was one which was repeatedly confirmed. Fig. 1 shows an example in which 5 mg. and 2 mg. thiopentone were added to a bath of 8 ml., so that the concentrations were $0{\cdot}6 \times 10^{-3}$ and $0{\cdot}25 \times 10^{-3}$ g. per ml.; these were high concentrations.

Perfusion of Vessels of Rabbit Ear

We next observed that when thiopentone was injected into the fluid entering the central artery on the dorsum of the rabbit ear it caused a diminution of outflow as a first effect, which was often, though not always, followed by an increase in outflow. In fig. 2a the injection of 0·001 μg. noradrenaline caused vasoconstriction shown by the fall in outflow, and then the injection of 50 μg. thiopentone caused vasoconstriction followed by dilatation. Thiopentone is alkaline; and the solution we injected had a pH of 8·65, which might have been responsible for the vascular changes. When, however, we injected the same volume of Locke's solution adjusted to the same pH, there was no change in outflow.

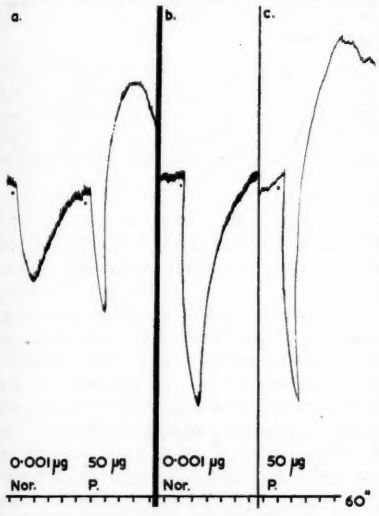

Fig. 2—Record of venous outflow from a rabbit ear perfused with Locke's solution.

In (*a*) the outflow fell after the injection of 0·001 μg. noradrenaline into the artery. When this effect was finished, 50 μg. thiopentone was injected causing constriction followed by dilatation. Cocaine hydrochloride (5 μg. per ml.) was then added to the perfusion fluid. The injections were repeated. The constrictor effects of noradrenaline and also of thiopentone were increased to a similar extent.

We wished to discover if the constriction caused by thiopentone was similar to that caused by noradrenaline, and we therefore determined how it was affected by the presence of cocaine. Cocaine increases the effect of adrenaline (Fröhlich and Loewi 1910), and it increases the effect of noradrenaline also. We added cocaine hydrochloride to the solution perfusing the ear, the concentration being 5 μg. per ml. This was allowed to perfuse the ear overnight. Figs. 2b and c show the effect on the next morning when the same injections of noradrenaline and of thiopentone were made again. In both cases the fall in venous outflow was about twice the fall on the previous day. We observed in three experiments that cocaine had a similar potentiating effect on the constrictor action of thiopentone to that on the constrictor action of noradrenaline. In one of these experiments a concentration of cocaine equal to 40 μg. per ml. increased the constrictor actions of thiopentone and of noradrenaline threefold.

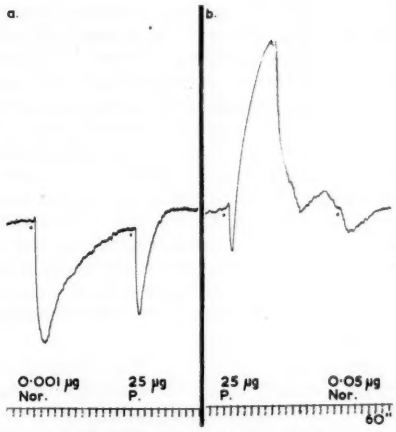

Fig. 3—Records of venous outflow.

In (*a*) the injection of 0·001 μg. noradrenaline and of 25 μg. thiopentone caused a fall in outflow. Tolazoline was then added to the fluid perfusing the ear in a concentration of 5 μg. per ml. In (*b*) the effect of 25 μg. thiopentone was reversed, and the effect of 0·05 μg. noradrenaline was abolished.

These observations were consistent with the view that the effect of thiopentone in causing constriction was due to the liberation of noradrenaline from a store in or near the vessel walls.

Action of Tolazoline

We next determined how the constrictor action of thiopentone was modified when tolazoline (' Priscol ') was introduced into the perfusing solution. An example of the effect obtained is shown in fig. 3. In (*a*) the constric-

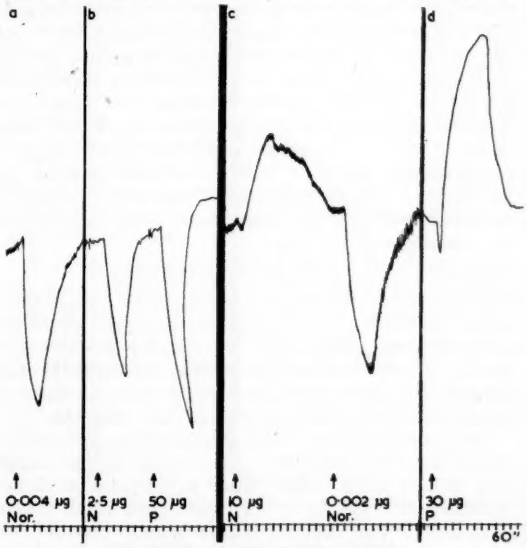

Fig. 4—Records of venous outflow.

(*a*) and (*b*) show the constrictor responses, with fall in venous outflow, to 0·004 μg. noradrenaline, 2·5 μg. nicotine acid tartrate (N), and 50 μg. thiopentone (P). These were in a normal ear. (*c*) and (*d*) show the responses evoked by the same substances in an ear from a rabbit treated with reserpine. Noradrenaline caused constriction, but nicotine and thiopentone caused dilatation.

tions caused by 0·001 μg. noradrenaline and by 25 μg. thiopentone were recorded, and then tolazoline was added to the fluid perfusing the ear. This substance reduces the effect of noradrenaline and sometimes reverses it so that noradrenaline causes dilatation instead of constriction. It regularly reverses the action of adrenaline. In the experiment shown in fig. 3, during the infusion of tolazoline the injection of thiopentone was largely reversed (fig. 3b). There was a small initial constrictor phase followed by dilatation. The effect of a 50-times larger dose of noradrenaline than that given in fig. 3a was to cause only a very slight constriction. This result further supported the view that the action of thiopentone in causing constriction was due to the liberation of noradrenaline.

Effect of Reserpine

Observations were made by Burn and Rand (1957, 1958b) on the store of noradrenaline in artery walls. When they took the thoracic aorta from a series of rabbits and ground it up and extracted it, they found that it contained noradrenaline in a mean amount of 0·5 μg. per g. If, however, they took the thoracic aorta from rabbits injected with reserpine they found less than one-fifth of this amount. Reserpine had depleted the store in the artery wall. They also made observations on the vasoconstrictor action of nicotine in the perfused rabbit ear by the method now used for thiopentone and found that nicotine caused constriction in the ears of normal rabbits, but not in the ears of rabbits which had been treated with reserpine. They concluded that nicotine caused constriction by releasing noradrenaline, because it lost its constrictor action when the store of noradrenaline was depleted.

We have made many observations to determine the effect of thiopentone in the ears of rabbits treated with reserpine. It was not possible to test the effect in the same ear before and after reserpine treatment, and the comparison was made between the ears of different animals. Fig. 4 gives an example taken from a normal ear and an ear from a reserpine-treated rabbit examined on the same day. In figs. 4a and b the constrictor effect in the normal ear of noradrenaline, nicotine, and thiopentone is shown. In figs. 4c and d the same substances were tested in the ear from a reserpine-treated rabbit. In this rabbit noradrenaline produced constriction, but nicotine and thiopentone caused dilatation. These observations also supported the view that thiopentone caused constriction by releasing noradrenaline.

Vascular Spasm Caused by Other Substances

In his survey of cases of vascular spasm due to intra-arterial injection of thiopentone, Cohen (1948) mentioned other substances which have been found to have the same action. These include ethanolamine, sodium iodide, and quinine. He drew attention to the absence of any record of vascular spasm being caused by hexobarbitone.

We therefore tested these substances in the perfused rabbit ear. We found that ethanolamine, sodium iodide, and quinine had a similar action to thiopentone, though sodium iodide was active only when given in an amount of 2–4 mg. The effect of sodium iodide, however, was not due to the unspecific effect of the amount injected because the same amounts of sodium chloride did not cause constriction. Fig. 5 shows the constrictor action of 1·5 μg. ethanolamine, of 4 mg. sodium iodide, and of 50 μg. quinine.

The action of hexobarbitone was also carefully tested,

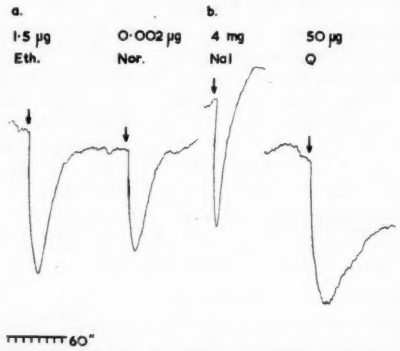

Fig. 5—Records showing constriction caused by 1·5 μg. ethanolamine (Eth.), 0·002 μg. noradrenaline (Nor.), 4 mg. sodium iodide, and 50 μg. quinine sulphate.

but it failed to cause constriction except in a high dose. Whereas in more than 40 experiments thiopentone caused constriction in doses of from 25 to 50 μg., hexobarbitone in a dose of 1 mg. caused only slight constriction. The comparison showed that it was about 60 times weaker than thiopentone.

Perfusion in the Dog and the Cat

Attempts were made to observe the occurrence of arterial spasm in the perfused vessels of the dog and of the cat. Three experiments were carried out in which the hindleg of the dog was perfused with blood by a Dale-Schuster pump. Thiopentone in 10% concentration was then injected into the cannula tied in the femoral artery, the volume injected being 1 ml. In none of the experiments was an increase in arterial tone observed. It seemed possible that one explanation of this failure was that the vessels perfused were mainly the vessels of muscles, and that the spasm might be seen more easily in skin vessels. We therefore carried out an experiment in which we perfused the tail of a cat, using Locke's solution. In this experiment also the injection of thiopentone in 10% solution failed to increase the degree of arterial constriction.

Discussion

These observations show that thiopentone causes contraction of isolated strips of the aorta of the rabbit and causes constriction when it is injected into the vessels of the perfused rabbit ear. They further strongly suggest that this constriction is due to thiopentone causing the release of noradrenaline, which has been found in the walls of the arteries, or which is present in chromaffin tissue adjoining the walls. These observations do not provide any obvious explanation of the sensation of burning pain which has followed the intra-arterial injection of thiopentone in man, or the complete thrombosis of arteries which has also been recorded. With regard to the burning pain, this has been found to follow intra-arterial injection of acetylcholine (Harvey et al. 1941), and acetylcholine has been shown to cause constriction due to the release of noradrenaline in the vessels of the perfused rabbit ear (Burn and Rand 1957, 1958b).

Burning pain in the limbs leading to gangrene of the extremities is a characteristic of ergot poisoning. The effects of the intra-arterial injection of thiopentone in man have been described as similar to those of frostbite. There is intense spasm or thrombosis in the distal arteriocapillary loops, and terminal gangrene of the fingertips has occurred in some cases.

Suggestive evidence of a connection between the constrictor action in the rabbit-ear vessels and the pathological changes in man also comes from the different compounds which have been examined. Quinine and ethanolamine, which are used to cause thrombosis of varicose veins, and sodium iodide have all caused vascular accidents after intra-arterial injection. They are all constrictor substances in the rabbit ear, while hexobarbitone, which has never caused a vascular accident, is almost devoid of constrictor action in the rabbit ear.

Possibly the demarcation of a group of substances with the common property of releasing noradrenaline from structures—most likely chromaffin cells—in or near the vessel walls will be a first step towards discovering how their action leads to thrombosis.

Summary

Thiopentone has on occasion been injected intra-arterially and has caused burning pain, followed in some cases by vascular thrombosis.

Examination of thiopentone has shown that it causes contraction of isolated arterial strips, and constriction of the perfused vessels of the rabbit ear. This constriction was found to be due to release of noradrenaline from structures in or near the artery wall, since it was increased by cocaine, and abolished or even reversed by tolazoline, and slight or absent in ears from rabbits treated with reserpine. The constriction was not due to the alkaline pH of the solution.

Other substances which have also caused vascular thrombosis—quinine, ethanolamine, and sodium iodide—were likewise found to constrict the vessels of the rabbit ear. Hexobarbitone, which has not caused vascular thrombosis, had almost no constrictor action in the rabbit ear.

Attempts to observe a similar constrictor action due to thiopentone in the perfused dog's hindleg and in the perfused cat's tail were unsuccessful.

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CHANGES IN COAGULABILITY OF THE BLOOD DURING VARIOUS PHASES OF ISCHÆMIC HEART-DISEASE

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COAGULABILITY of the blood was previously compared in patients with ischæmic heart-disease and healthy controls of the same age and sex (McDonald 1957, McDonald and Edgill 1957). There were significant differences between the mean values for the two groups in relation to thromboplastin-generation, platelet stickiness, fibrinogen-estimation, and prothrombin-time (Russell's-viper venom, 'Stypven'); these differences indicated hypercoagulability of the patients' blood.

The patients initially studied had angina pectoris on exertion. Although cardiac infarction had occurred previously in some of the cases, it was recent in none.

Several important questions arose from these findings. The first was whether hypercoagulability was of a different order in cases of simple angina of effort, acute coronary insufficiency (Master et al. 1947), and recent cardiac infarction. The second was whether acute coronary insufficiency and cardiac infarction themselves modified coagulation. The third question was what variation in coagulability occurred in patients who did not experience an acute phase of the disease, and in healthy controls, on repeated testing. The present investigation was made to decide these points.

Material

In the original study patients with either acute coronary insufficiency or cardiac infarction had deliberately been excluded. It was thought that enough patients might develop acute coronary insufficiency or cardiac infarction, while their blood coagulation was being repeatedly tested, to enable these acute phases of ischæmic heart-disease to be investigated. In fact so few did develop these states that separate patients had to be studied.

Study of acute coronary insufficiency and cardiac infarction.—22 healthy men and 30 men with angina pectoris on exertion were compared with 7 cases of acute coronary insufficiency and 10 of cardiac infarction. All these patients were male except 2 with acute coronary insufficiency and 2 with cardiac infarction. The healthy men were aged 41–61 (average 51·0); the patients with angina pectoris 42–62 (average 53·2); those with acute coronary insufficiency 43–71 (average 57·6); and with cardiac infarction 53–70 (average 64·4).

Repeated tests.—15 healthy men and 29 men with angina pectoris on exertion were studied. The healthy men were aged 41 to 61 (average 51·7), and the patients 42–62 (average 53·3).

Procedure.—Patients with acute coronary insufficiency and cardiac infarction were studied in a fasting state on admission to hospital. The patients with acute coronary insufficiency were suffering from this syndrome at the time of admission. Cardiac infarction had occurred in the others from less than twenty-four hours to thirteen days before they were studied.

The healthy men and the patients with angina pectoris who were repeatedly tested were ambulant and attended as outpatients for samples of blood to be taken at 9.30 A.M. under standard conditions.

They were instructed to have only a light breakfast—i.e., tea or coffee and toast, with no cream and very little butter, on the morning of their test. Blood was withdrawn from an antecubital vein into an oiled syringe; samples were accepted only if there had been a clean venepuncture and an uninterrupted flow of blood into the syringe.

The tests of blood coagulation given below were repeated at intervals of from two to thirty-one weeks, the average being fourteen weeks.

Method

Blood-coagulation.—In the study of acute coronary insufficiency and cardiac infarction blood coagulation was investigated in relation to platelet-count, estimation of platelet stickiness, fibrinogen estimation, thromboplastin-generation test, and prothrombin-time (Russell's-viper venom, stypven), In the repeated tests blood coagulation was similarly studied, except the prothrombin-time was omitted.

Technical details.—All tests of blood coagulation were performed as described by McDonald and Edgill (1957), with

the modifications later incorporated (McDonald and Edgill 1958). Platelet stickiness was estimated at 20 minutes only. In the thromboplastin-generation test a fresh chloroform extract of brain was made for the later tests. A comparable dilution curve was prepared for the new extract, using the pooled plasma and serum of the same 6 healthy subjects as before.

Results

Acute Coronary Insufficiency and Cardiac Infarction

The results of the coagulation tests in this study are shown in the scattergram (see figure) and in table I. The range in normal subjects and patients with angina pectoris, also the changes occurring with acute coronary insufficiency and cardiac infarction, are given.

Platelet Stickiness

In the stickiness test, values for platelets removed at twenty minutes, expressed as a percentage of the initial count, were 57 to 88 (mean 80%) for normals; 48 to 76 (mean 60) in angina pectoris; 57 to 64 (mean 61) in acute coronary insufficiency; and 36 to 63 (mean 51) in cardiac infarction. The difference between the means for normals and for each group of patients was significant at the 1% level.

A difference significant at the 1% level occurred between patients with angina pectoris and those with acute coronary insufficiency, when compared with those with cardiac infarction. Thus stickiness increased significantly from normals to patients with angina pectoris, and from them to patients with cardiac infarction. Findings in acute coronary insufficiency were not significantly different from those in angina pectoris.

Fibrinogen

In the fibrinogen-estimation values for normals were 0·050 to 0·090 (mean 0·061) ml. in 2 ml. plasma; 0·055 to 0·090 (mean 0·076) in angina pectoris; 0·070 to 0·090 (mean 0·078) in acute coronary insufficiency; and 0·075 to 0·011 (mean 0·094) in cardiac infarction. The difference between the means for normals and for each group of patients was significant at the 1% level.

A difference significant at the 1% level occurred between patients with angina pectoris and those with acute coronary insufficiency, when compared with those who had cardiac infarction. Fibrinogen levels, therefore, increased from normals to patients with angina pectoris, and from those to patients with cardiac infarction. Levels in acute coronary insufficiency were not significantly different from those in angina pectoris.

Thromboplastin-generation

In the thromboplastin-generation test, the peak percentage achieved in normal subjects was from 85 to 122 (mean 105); in angina pectoris 108 to 130 (mean 119); in acute coronary insufficiency 112 to 120 (mean 116); in cardiac infarction 115 to 145 (mean 125). The difference between the means for normals and for each group of patients was significant at the 1% level, excluding the patients with acute coronary insufficiency, when the difference was significant only at the 5% level. This is likely to have been due to the small number of patients in this group.

A difference nearly significant at the 5% level occurred between patients with angina pectoris and those with cardiac infarction. No significant difference was found between patients with angina pectoris and acute coronary insufficiency, nor between the latter and those with cardiac infarction. Peak percentage levels therefore increased from normal subjects to patients with angina pectoris and from those to patients with cardiac infarction.

TABLE I—PLATELET-COUNTS IN NORMAL SUBJECTS AND IN PATIENTS WITH ANGINA PECTORIS, ACUTE CORONARY INSUFFICIENCY, AND CARDIAC INFARCTION

—	Number of subjects	Mean of platelet-counts, per c.mm. whole blood, in thousands *	Standard error	Pooled standard deviation within group
Normal subjects	22	256·0	10·7	50·2
Angina pectoris	30	245·7	9·2	
Acute coronary insufficiency	7	314·4	19·0	
Cardiac infarction	10	280·5	15·9	

* For significance of differences see text.

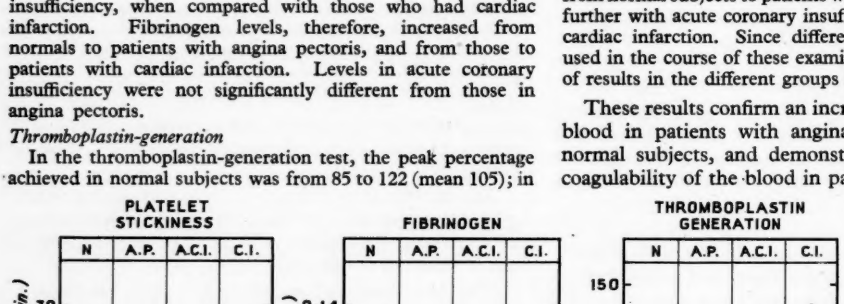
Platelet-counts

Mean values for platelet-counts are shown in table I. In acute coronary insufficiency the mean platelet-count was significantly higher, at the 5% level, than in normal subjects and in patients with angina pectoris. The mean count in patients with cardiac infarction was intermediate, and did not differ significantly from the others.

Prothrombin-time

Using stypven, the prothrombin-time appeared to shorten from normal subjects to patients with angina pectoris, to shorten further with acute coronary insufficiency, and even more with cardiac infarction. Since different batches of stypven were used in the course of these examinations, an exact comparison of results in the different groups is not merited.

These results confirm an increase in coagulability of the blood in patients with angina pectoris compared with normal subjects, and demonstrate a further increase in coagulability of the blood in patients with cardiac infarction. Patients with acute coronary insufficiency, in this respect and in this study, appeared to have a level of coagulability of the blood comparable to that found in patients with angina pectoris on exertion only, and less than that found in cardiac infarction.



Repeated tests.—Mean values and the variation in normal subjects and in patients with angina pectoris for platelet-counts, estimation of platelet stickiness and fibrinogen, and thromboplastin-generation, are shown in table II. The difference between

TABLE II—REPEATED TESTS OF BLOOD COAGULATION: MEAN VALUES AND VARIATION IN NORMAL SUBJECTS AND PATIENTS WITH ANGINA PECTORIS

—	Normal subjects			Patients			Significance of ratio of standard deviations
	Mean	Subjects (with no. of readings)	Standard deviation within normals (with degrees of freedom)	Mean	Patients (with no. of readings)	Standard deviation within patients (with degrees of freedom)	
Platelets (per c.mm. whole blood)	264,500	15 (*43*)	16,300 (*28*)	248,200	20 (*61*)	22,500 (*41*)	5%
Platelet stickiness (% of initial count remaining at 20 min.)	79·8	13 (*26*)	5·9 (*13*)	60·6	13 (*39*)	5·1 (*26*)	N.S.
Fibrinogen (ml. in 2 ml. plasma)	0·062	15 (*37*)	0·008 (*22*)	0·076	25 (*71*)	0·010 (*46*)	N.S.
Peak thromboplastin (%)	104·4	15 (*31*)	6·0 (*16*)	117·4	20 (*60*)	5·7 (*40*)	N.S.

N.S. = not significant.

the means of normals and patients, previously shown in these tests, remained unaltered on repeated testing, and indicated hypercoagulability in the patients. The variation within normals and patients did not differ significantly, except in the total platelet-count. In this the ratio of standard deviations was significant at the 5% level, and the total platelet-count varied more in patients than in normals.

From repeated tests of platelet stickiness, patients and normal subjects can be almost completely separated. Platelet stickiness at 20 minutes of 65% or less was strongly in favour of ischæmic heart-disease, if other factors associated with increased stickiness were absent (see below).

Discussion

These studies confirm the hypercoagulability of the blood that we have described previously in patients with angina pectoris, and show that it is persistent on repeated testing. They also reveal that hypercoagulability is greater after cardiac infarction, and are in full accord with the clinical observation that patients with ischæmic heart-disease have an increased tendency to thrombosis.

Relative hypercoagulability of the blood exists in some normal people, but there is no evidence as yet that this predisposes to ischæmic heart-disease. Hypercoagulability may be an effect of ischæmic heart-disease rather than a cause. This is not to deny that temporary hypercoagulability, followed by thrombosis, might not initiate the disease, nor that previous hypercoagulability might not increase with it.

Tests of blood coagulation which are performed in vitro must be considered in relation to coagulability and thrombosis in vivo. They may be assumed to reflect coagulability of the blood in vivo, and thrombosis is likely to be associated with hypercoagulability. Absolute figures in any of the tests may permit only limited interpretation; the comparison of normal subjects with patients, or of patients in different phases of their disease, is more valuable. Various factors which might affect blood coagulation, such as rest in bed, age, and menstruation, were investigated.

The amount of rest in bed that any of the patients had was not found to affect the tests of blood coagulation that were used. Increased thromboplastin-generation and platelet stickiness were more often found in older subjects, but in the present study the ages of normal subjects and patients were similar. Blood coagulation may fluctuate throughout the menstrual cycle; menstrual women were excluded from the present study.

Increased platelet stickiness is not specific for ischæmic heart-disease; we have found it, for example, in luetic aortitis, and Wright (1942) found it after parturition and surgery. Patients with other known causes for increased platelet stickiness were also excluded. Increased plasma-fibrinogen after cardiac infarction is now well recognised (Meyers 1948), and is possibly due to tissue destruction; Losner and Volk (1956) found it raised in cardiac infarction but not with acute coronary insufficiency. Repeated platelet-counts varied more in patients with ischæmic heart-disease than in normal subjects; this may be related to the increase found with acute coronary insufficiency, although this in itself remains unexplained. Increased platelet stickiness may merely reflect the presence of intravascular thrombosis (Bobek and Cepelak 1958), and we have found it increased in extracardiac thrombotic conditions. Thus increased stickiness in ischæmic heart-disease may indicate a predisposition to thrombosis, the actual presence of intravascular thrombosis, or both.

Heparin is known to reduce platelet stickiness, and the platelet-stickiness test might therefore indicate the amount of available heparin in the subject. However, comparable differences in stickiness were found between patients and controls when both sodium citrate and potassium oxalate were used as anticoagulants in the test. Nevertheless, the studies of Ulutin and Sestakof (1957) do suggest either underproduction or increased utilisation of heparin in ischæmic heart-disease; intravenous heparin depressed thromboplastin-generation for much longer in normal subjects than in patients with ischæmic heart-disease.

Various anticoagulants act differently in restoring hypercoagulability of the blood towards normal.

Thus heparin rapidly depresses thromboplastin-generation to normal levels and below, and platelet stickiness is reduced towards normal, although the effect is less. Phenindione affects both these tests less. In anticoagulant therapy with phenindione, the optimum amount of the drug is usually judged by the prothrombin-time. However, the amount of anticoagulant needed probably varies with the degree of hypercoagulability. It is not surprising that some patients, in whom anticoagulant therapy with phenindione appears well controlled by the prothrombin-time, develop thrombosis.

Ideal anticoagulant therapy might be based on the titration of the right anticoagulant against the clotting factors which are known to be abnormal.

O'Brien (1956) thinks it likely that the activity of platelets in coagulation is due to ethanolamine phosphatide or some related compound; but for the present it may be accepted that " not enough is known about the connection between clotting and thrombosis to decide whether or not the part played by fats in blood coagulability is relevant to the mechanism of thrombosis " (Poole 1958). Modification of the diet may, however, produce an anticoagulant effect. Diminished platelet stickiness and lowered serum-cholesterol have been found after the rice-fruit diet (McDonald 1958, McDonald and Edgill 1958), but there was no evidence that the change in stickiness was due to the reduction of cholesterol, as

opposed to some other metabolic change. When serum-cholesterol was lowered by corn oil, in hypercholesterolæmic patients, coagulability of the blood remained unaltered (McDonald, Edgill, and Murdoch, unpublished).

Anticoagulant therapy has made repeated examination of coagulation after cardiac infarction impracticable in the present patients. Past observations, however, suggest that these changes may be greatest one or two days after infarction, and gradually return to the level found in patients with angina pectoris who have not had recent cardiac infarction (McDonald and Edgill, unpublished). There are at least three possible reasons for hypercoagulability after cardiac infarction. A phase of hypercoagulability may immediately precede infarction, initiate coronary thrombosis, and persist after the acute episode. On the other hand, hypercoagulability may merely reflect the presence of recent thrombosis, or be caused by tissue damage and intravascular stasis. The natural history of ischæmic heart-disease could be affected by hypercoagulability of the blood in different ways. Thus an increased tendency to mural thrombosis, leading to atherosclerosis (Duguid 1946), and a greater likelihood of complete arterial occlusion by thrombosis, would be expected if hypercoagulability is associated with an increased tendency to thrombosis.

In conclusion, there is clear evidence of phasic hypercoagulability when the blood of patients with ischæmic heart-disease is studied in vitro. This is entirely in keeping with a variable hyperthrombotic state, and ischæmic heart-disease is marked clinically by episodes of thrombosis. The possibility of heparin deficiency or overutilisation in the disease is being further investigated.

Summary

Coagulability of the blood, in relation to platelet-count, estimation of platelet stickiness, fibrinogen estimation, thromboplastin-generation, and prothrombin-time (Russell's-viper venom, ' Stypven '), was compared in 22 healthy men, 30 men with angina pectoris on exertion, 7 patients with acute coronary insufficiency, and 10 patients with cardiac infarction. All these patients were male except 2 with acute coronary insufficiency and 2 with cardiac infarction.

Values for platelet stickiness, thromboplastin-generation, and fibrinogen estimation significantly increased from healthy controls to patients with angina pectoris, and from these to patients with cardiac infarction. Findings in acute coronary insufficiency were not significantly different from those in angina pectoris, except that the platelet-count was higher in acute coronary insufficiency than in other groups. There were no other significant differences between groups, in respect of platelet-counts. Thus coagulability of the blood was higher in patients with angina pectoris than in healthy controls, and higher again in patients with cardiac infarction. Patients with acute coronary insufficiency appeared to have a level of coagulability comparable to that found in patients with angina pectoris on exertion only, and less than that found in cardiac infarction.

In 15 healthy men, and 29 men with angina pectoris on exertion, blood coagulation was similarly tested on repeated occasions. The hypercoagulability of the blood in patients with angina pectoris was confirmed. The variations within the groups of healthy controls and of patients did not differ significantly, except in the total platelet-count. This varied more in patients than in normals.

Observations on hypercoagulability of the blood in normal people, and on various factors which might affect blood coagulation (including rest in bed, age, the menstrual cycle, intravascular thrombosis, anticoagulants, diet, and serum-cholesterol) are presented.

The blood of patients with ischæmic heart-disease, studied in vitro, shows a phasic hypercoagulability which is entirely in keeping with a variable hyperthrombotic state.

The cooperation and advice of Dr. R. G. Macfarlane, F.R.S., and Dr. Rosemary Biggs have been of the greatest value throughout these investigations. We thank Dr. Paul Wood, director of the Institute of Cardiology, who has constantly supported this work; the physicians of the National Heart Hospital, and Dr. G. S. C. Sowry, who have allowed us to study their patients; Dr. Helen Payling Wright for advice on the platelet-stickiness test and for the loan of apparatus; Dr. P. Armitage and Dr. J. O. Irwin, who made the statistical analysis; Imperial Chemical Industries Ltd., for a grant which covered part of this investigation; Burroughs Wellcome and Co., for a supply of ' Stypven '; L. E. Pritchitt and Co. Ltd., for corn oil; the volunteers from the Prudential Assurance Company Ltd., who acted as controls; and Miss Lesley Murdoch, B.SC., for much assistance.

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INFLUENZAL PITUITARY DEPRESSION

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RECENT influenza epidemics have been marked by low mortality but high incidence. The symptoms have conformed with those usually found (Abrahams et al. 1919, Stuart-Harris 1953, Woodall et al. 1958). Outstanding among these symptoms is debility, comprising not only bodily discomfort but also impaired mental vitality persisting in some instances for many weeks.

I show here that influenzal debility may be associated with deficient anterior-pituitary function and relieved by administration of corticotrophin or steroids.

Material

In the autumn of 1958 4 patients were admitted to one medical ward with influenza; in 2 instances the diagnosis was confirmed serologically (table I). All presented a similar clinical picture, though the severity varied between the patients.

Symptoms

The illness was characterised by sudden onset, the outstanding symptoms being considerable fatigue and muscular weakness, severe dyspnœa, aching limbs, and mental depression.

Fatigue and Weakness

Drowsiness and a sensation of exhaustion were the most conspicuous symptoms and were present for periods ranging from four days to three weeks until relieved by treatment. Case 1 was so exhausted that he fell asleep several times during interrogation, and muscular weakness was so severe that a diagnosis of myasthenia gravis was considered and excluded after a subcutaneous injection of neostigmine failed to improve

muscular power. Case 2 was prevented from walking more than two consecutive paces by the sudden onset of muscular weakness, and he asserted that extreme weakness was the cause of urinary incontinence at the onset of his illness.

Dyspnœa

Considerable breathlessness on slight exertion was also a prominent symptom. Furthermore, attacks of urgent nocturnal dyspnœa had awakened all 4 patients from their sleep; the dyspnœa persisted for five to ten minutes, and in case 3 it was relieved by sitting upright with the legs over the side of the bed.

It is not surprising that these patients were sent into hospital with a tentative diagnosis of left ventricular failure. None of these patients, however, had orthopnœa, nor had they hypertension or valvular heart-disease. Case 1, who was the least troubled by dyspnœa, had the electrocardiographic pattern of an old cardiac infarction (coronary thrombosis had occurred a year previously) but there was no evidence of recent myocardial ischæmia. 3 patients (cases 2–4) had chronic bronchitis and emphysema, but the severity of dyspnœa was disproportionate to their physical and radiographic signs.

Paroxysmal cough was the least troublesome of symptoms. Only small quantities of white frothy sputum were expectorated, but transient slight blood-streaking of the sputum occurred in case 2.

Aching Limbs

Generalised muscular aching was not particularly severe; it was most evident in the thighs, the shoulder-girdles, and the lumbar paravertebral muscles. With bed rest, backache was relieved first whilst aching in the trapezii was the last to subside. The sequence of relief suggested that these pains were due to muscle weakness and fatigue, those muscles which received greatest support by bed rest being the first to benefit.

TABLE I—AGE, BLOOD-PRESSURE, AND ASSOCIATED CONDITIONS IN PATIENTS WITH INFLUENZAL DEBILITY

Case no.	Sex	Age (yr.)	Blood-pressure (mm. Hg)	Influenza-A complement-fixation test	Associated conditions
1	M	60	105/75	Positive 1 in 32	Myocardial infarction one year previously
2	M	66	115/70	Not done	Duodenal ulcer twenty years (hæmatemesis on 2 occasions); chronic bronchitis and emphysema
3	M	61	*100/65	Not done	Chronic bronchitis and emphysema
4	M	54	110/80	Positive 1 in 32	Chronic bronchitis and emphysema; partial gastrectomy ten years previously

* Blood-pressure nine days after admission; initially 140/90.

Mental Depression

Mental depression was present in varied degree in all 4 patients. Reduced mental vitality and emotional depression were most evident in case 1, who appeared uninterested in his illness and surroundings but despite apparent paucity of feeling was, during examination, so depressed that tears welled into his eyes and rolled down his cheeks. So profound were his symptoms that an electroencephalogram was done. This showed an unstable alpha rhythm and much irregular activity over both hemispheres. Large slower waves, without focal distribution, were also seen occasionally. Overbreathing was impossible. The record was reported "abnormal and of unusual type suggesting the possibility of encephalitis". A similar pattern was obtained when the encephalogram was repeated nine days later. Clinically he had no localising neurological abnormalities, but slight muscular twitching was seen in the face and limbs. This patient was also found to have hepatomegaly with abnormal liver-function tests (serum-bilirubin 1·5 mg. per 100 ml., Kunkel 10 units, alkaline phosphatase 8 units, thymol turbidity 3 units, total serum-proteins 6·5 g. per 100 ml. [albumin 4·1 g., globulin 2·4 g., per 100 ml.]). With evidence of neurological and hepatic disorder he resembled the cases recently described by Kapila et al. (1958). It is surprising that this combination of neurological and hepatic involvement has not often been recorded previously in patients with influenza since Henle and Henle (1946a and b), investigating the toxic effects of influenza virus in laboratory animals, found the liver and brain to be the most susceptible organs.

TABLE II—URINARY EXCRETION OF 17-KETOSTEROIDS AND CORTICOIDS BEFORE AND AFTER CORTICOTROPHIN ADMINISTRATION IN PATIENTS WITH INFLUENZA

Case no.	Before corticotrophin (mg. per day)		After corticotrophin (mg. per day)	
	17-ketosteroids	Corticoids	17-ketosteroids	Corticoids
1	<1	4·2	3·8	8·5
2	1·1	4·5	7·5	14·6
3	2·6	6·7	9·9	21
4	4·1	..	16·9	..

Other Symptoms

3 patients (cases 2–4) sweated excessively at night and profusely with slight exertion. Transient attacks of vertigo with change of posture or attempted exertion, which occurred in 2 patients (cases 3 and 4), were attributed to postural hypotension. Case 3 became pale, sweated, and felt faint when sitting upright in bed; and on standing his blood-pressure became unrecordable and he fainted.

Specific Investigations

Mental and physical fatigue were such prominent symptoms in these patients that a diagnosis of Addison's disease was suggested. All 4 patients had low blood-pressures (table I), and 2 (cases 3 and 4) had postural hypotension—a common feature in Addison's disease (Ghrist 1929, Talbot et al. 1952).

This clinical evidence prompted investigation of adrenocortical function:

1. The urinary excretion of 17-ketosteroids and corticoids was assessed before and after a three-day course of intramuscular corticotrophin 40 units q.d.s. In each instance the urinary steroid excretion was subnormal, but increased values were obtained after administration of corticotrophin (table II).

2. Serum-electrolyte estimations (table III) revealed hyponatræmia associated with a normal serum-potassium level in 3 patients (cases 2–4).

The blood-urea level, estimated in 3 patients, was raised in 1 (case 3). A Robinson-Power-Kepler test, performed on case 4, was positive (factor A = 14).

These results supported the possibility of adrenocortical insufficiency but indicated that the primary deficiency was at anterior-pituitary rather than adrenocortical level. Normal electrolyte values in case 1 were attributed to a maintained baseline aldosterone secretion, which is known to continue independent of anterior pituitary function (Thorn et al. 1957).

Treatment

Noticeable improvement occurred in all 4 patients whilst receiving the three-day "test" course of intramuscular corticotrophin, and in case 3 no further treat-

TABLE III—BLOOD-ELECTROLYTE (MEQ. PER LITRE) PLASMA ALKALI RESERVE (VOLS. CO_2), AND BLOOD-UREA (MG. PER 100 ML.) LEVELS IN PATIENTS WITH INFLUENZA

Case no.	Serum-sodium	Serum-potassium	Plasma-chloride	Plasma alkali reserve	Blood-urea
1	148	4·2	109	18·3	28
2	137	5·7	..	..	..
3	130	4·0	91	22·8	62
4	130	5·9	99	22·8	26

ment was required. Asthenia disappeared, dyspnœa vanished, they became more alert, and they lost their mental depression. In 3 patients (cases 1, 2, and 4) symptoms recurred within two days of corticotrophin being discontinued, and these patients were given prednisolone 5 mg. t.d.s. for twenty-four hours followed by 2·5 mg. t.d.s. for periods ranging from two to three weeks. During this treatment all symptoms disappeared, they rapidly gained strength, and they were up and about in the ward free from dyspnœa; serum-electrolyte levels, previously abnormal, reverted to normal. The prednisolone dosage was then reduced over a period of two days, during which time and for a further three days they received intramuscular corticotrophin gel 60 units every morning. Each patient, on admission, was given a five-day course of penicillin to combat existing respiratory infection and also as a prophylactic measure whilst receiving steroid therapy.

The effects of steroid therapy were particularly striking in case 1, who was extremely depressed. Improvement in mental function was initiated by administration of corticotrophin, and was especially noticeable during prednisolone therapy; and his mental state was normal when he was discharged after three weeks' treatment. When seen as an outpatient a month later, he had no influenzal sequelæ and electroencephalography showed that the previously recorded abnormalities had disappeared.

Discussion

The value of steroid therapy in the treatment of influenza has been disputed.

Thus Walker et al. (1958) were unimpressed by steroid therapy during the 1957 Asian influenza pandemic. Good results were claimed by Rotem (1957) and by Plaza de los Reyes and Cruz-Coke (1957), but Gunn (1957) considered that steroid drugs were contraindicated in the treatment of influenza. Oswald et al. (1958) described 27 patients with fulminating influenza who received steroid therapy; 17 died, but 8 of these deaths occurred within twenty-four hours of admission to hospital. Oswald et al. concluded "that the survivors were those with a reasonably free airway and comparatively little radiological evidence of consolidation who responded promptly to a combination of hydrocortisone and antibiotics".

Steroid drugs have been administered in influenza because of the necessity to combat the circulatory collapse associated with severe toxæmia. It has been suggested that toxæmia provokes adrenal damage, but postmortem evidence of adrenal lesions is rare in influenza. Among 24 necropsies in the report of the Public Health Laboratory Service (1958) adrenal hæmorrhage was noted on only 8 occasions.

That anatomical adrenal damage is uncommon in those who die with fulminating influenza is not surprising, since in the present series, although clinical and biochemical evidence indicated adrenocortical insufficiency, this was due to a primary reduction of anterior-pituitary function (table II).

Anterior-pituitary suppression could have resulted from direct damage by the virus to the pituitary or its higher controlling centres. Evidence of encephalopathy was present in case 1, who had the lowest urinary steroid excretion. The rapid improvement in mental function and correction of electroencephalographic abnormalities in this patient following steroid therapy suggests, however, that steroid deficiency per se rather than brain damage by the influenzal virus might be partly responsible for the encephalopathy. Indeed this explanation could account for the inability to isolate the virus from the brain in laboratory animals (Henle and Henle 1946a and b) and in patients who died with so-called encephalitis during the Asian influenza epidemic (Dunbar et al. 1958, Horner 1958, Flewett and Hoult 1958, Dubowitz 1958, Smith 1958). Flewett and Hoult (1958) preferred the term influenzal "encephalopathy" to encephalitis; they suggested that encephalopathy had resulted from severe anoxæmia and venous congestion associated with hæmorrhagic pneumonia. To these possible causes of encephalopathy Oswald et al. (1958) would add carbon-dioxide retention and "general toxæmia", in which instance they believed that "the adrenals may play a part". In the present series the association of disordered mental function with adrenocortical deficiency and its correction by steroid administration suggests a relationship between the mental state and adrenocortical activity. The influence of adrenocorticoids on carbohydrate metabolism might explain this relationship, since the functional ability of nerve-cells depends on a continuous supply of available glucose. Thus adrenocortical deficiency by impairing nerve-cell function could reduce pituitary stimulation from higher centres, thereby reducing endogenous corticotrophin production and so establish a vicious circle which would prolong postinfluenzal debility.

Histologically, extensive hæmorrhages into the white matter of the brain have been reported in a few cases (Crawford 1954, McGill and Goodbody 1958); but in most fatal cases of "influenzal encephalitis" the brain is intensely congested and œdematous (Giles and Shuttleworth 1957), early microglial proliferation may be seen, but perivascular cuffing does not occur. The same intense congestion and œdema is found in the lungs and trachea, even in those cases in which the lungs are shown to be bacteriologically sterile. In so far as adrenocorticoids are anti-inflammatory and antiexudative factors they might be expected to suppress this congestion and exudation phenomena in the brain and lungs, thereby improving mental function and relieving dyspnœa.

Neither anoxia, carbon-dioxide retention, venous congestion, nor direct damage by the virus could account for the anterior-pituitary insufficiency in the present series. It is perhaps significant that all 4 patients had a pre-existing illness (table I) which was likely to have created long-continued demands on the pituitary-adrenal mechanism. In such circumstances superadded infection might exhaust already depleted anterior-pituitary reserves. On the level of these reserves and their ability to stimulate the adrenal cortex would depend the severity of the debility and the effectiveness of steroid therapy in the treatment of influenza.

Summary

In each of 4 patients with influenza a similar pattern of symptoms, consisting of fatigue, muscular weakness, severe dyspnœa, aching limbs, and mental depression associated with a low blood-pressure, suggested adrenocortical insufficiency.

Determination of serum-electrolyte and urinary-steroid excretion levels supported this view, but correction of hyponatræmia and increased urinary steroid excretion following corticotrophin administration indicated that adrenocortical insufficiency was secondary to reduced anterior-pituitary activity.

Rapid improvement occurred in each patient during administration of corticotrophin and later of prednisolone. In 1 patient severe mental depression and electro-

encephalographic abnormalities disappeared following steroid therapy.

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ASIAN INFLUENZA WITH ADRENOCORTICAL INSUFFICIENCY

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THE 1957 wave of epidemic of influenza swept over the town of Malmö in October and November. Malmö General Hospital, the only hospital in the town, serves a population of about 220,000. During the epidemic 8117 cases of influenza were reported to the Board of Health. The true number of cases was, of course, much greater. In Malmö influenza or one of its complications caused a total of 10 deaths. Of these, 9 occurred among the 220 patients with influenza who had been admitted to hospital (see accompanying table).

Cases 1 and 2 died with untreated Addison's disease, and case 3 with untreated panhypopituitarism. Cases 1 and 3 died despite intense replacement therapy after admission; case 2 died before reaching hospital and had thus not received replacement therapy. In case 4 examination four years previously had suggested decreased adrenocortical reserve—an assumption supported later by the finding of adrenocortical atrophy at necropsy. Furthermore, case 5, who died from perforated gastric ulcer and influenza, also had adrenal failure, secondary to long-continued treatment of rheumatoid arthritis with cortisone; the adrenal insufficiency certainly contributed to the fatal outcome. Thus, at least 4 and probably 5 of the deaths were in patients with untreated or undertreated adrenocortical insufficiency. Of the other deaths, 2 were in elderly patients with arteriosclerotic heart-disease and 1 in a patient with severe diabetic nephropathy.

Discussion

The prognosis of Asian influenza is widely believed to be poorest in patients with cardiac and/or pulmonary insufficiency. In our series, however, the death-rate was much higher in patients with untreated adrenocortical insufficiency. Resistance to Asian influenza thus appears to be lowered more by untreated adrenocortical insufficiency than by chronic cardiac or respiratory disease. Of 5 further patients with adrenocortical insufficiency who were receiving adequate substitution therapy, the infection was mild in 4 and really severe in only 1. In addition, of 12 patients with adrenocortical insufficiency vaccinated against influenza at our hospital, only 2 developed influenza; and this was fairly mild in both. This suggests that adequate replacement therapy and/or vaccination will reduce any tendency to decreased resistance to influenza.

In all cases of severe influenza any suspected adrenal insufficiency should be compensated. Opinions differ on the wisdom of routine corticosteroid therapy in severe influenza. Plaza de los Reyes and Cruz-Coke (1957) and Rotem (1957) claimed good results; Walker et al. (1958) were not particularly impressed; and after observ-

FATAL CASES OF INFLUENZA

Case no.	Age (yr.)	Sex	Pre-existing diseases	Pathological diagnosis	Remarks
1	29	M	Addison's disease	Bronchopneumonia; adrenocortical atrophy	Adrenocortical insufficiency unknown before. Almost moribund on admission because of adrenal crisis. No response to vigorous treatment
2	65	F	Addison's disease	Tracheobronchitis; adrenocortical atrophy	Adrenocortical insufficiency diagnosed two years previously, but patient neglected treatment. Dead on admission
3	66	F	Sheehan's syndrome	Bronchitis and bronchopneumonia; fibrosis of anterior pituitary; atrophy of adrenals, thyroid, and ovaries	Neglected regular substitution therapy. No recent treatment with corticosteroids before admission. Poor response to intense replacement therapy
4	18	M	Gangliocytoma; adrenocortical insufficiency (secondary)	Bronchopneumonia; adrenocortical atrophy	..
5	31	F	Perforated gastric ulcer; rheumatoid arthritis; adrenocortical insufficiency due to cortisone treatment	Bronchitis and bronchopneumonia; rheumatoid arthritis; adrenocortical atrophy	Cortisone treatment of rheumatoid arthritis for 5 years
6	35	F	Diabetes mellitus with nephropathy	Bronchopneumonia	Diabetes of 12 years' duration
7	16	F	None	Bronchopneumonia	Four days' history of influenza. Moribund on admission and died within half an hour
8	75	F	Arteriosclerotic cardiovascular disease; cirrhosis of the liver	Tracheobronchitis	Severely ill before onset of influenza
9	68	F	Arteriosclerotic cardiovascular disease	Tracheobronchitis and bronchopneumonia	Severely ill before onset of influenza

ing 4 fatal cases treated in this way Gunn (1957) warned against this practice in the belief that it may interfere with immunity mechanisms. Reviewing the evidence for and against corticosteroid therapy in acute infections, Librach (1957) advocated caution.

In the event of a new wave of Asian influenza patients with adrenocortical insufficiency should be vaccinated and the adequacy of replacement therapy checked.

Summary

In the 1957 epidemic in Malmö, 220 patients were admitted to hospital with Asian influenza.

In the town influenza caused 10 deaths (9 in hospital). Of the 10 patients 4 had pre-existing untreated primary or secondary adrenocortical insufficiency, and a 5th had functional adrenocortical insufficiency.

In patients with adrenocortical insufficiency who were receiving full substitution therapy influenza ran a favourable course.

Apparently resistance to Asian influenza is lowered more by adrenocortical insufficiency than by cardiac and/or respiratory disease. In the event of a further wave of Asian influenza patients with adrenocortical insufficiency should be vaccinated and the adequacy of replacement therapy checked.

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WATER AND SODIUM IN TWO PSYCHOTICS

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BODY-WEIGHT often fluctuates notably in the course of a mental illness (Crammer 1957). Various opinions (Kalinowsky 1948, Post 1956) have been expressed on the origins of these fluctuations, but they have not been studied quantitatively or experimentally.

I have observed two chronic mental patients through a sequence of mental changes while controlling their food and fluid intake, and find that their weight losses correspond to periods of polyuria and greater sodium-chloride excretion. In them, therefore, a disturbance of the normal control of body-water accompanies the psychological disturbance in the full picture of the mental illness.

Methods

Patients were allotted a special nurse during the day, when they were up. At night they slept in siderooms under the general supervision of the ward night-nurse. Daily or twice-daily records of body-weight, resting pulse-rate, temperature, blood-pressure, and general behaviour were kept. All food offered was consumed: it was weighed beforehand and its general composition noted. Fluid intake was measured. Bowel actions were recorded and fæces weighed, while urine was collected as a series of twelve-hour or twenty-four hour specimens, for analysis of sodium and potassium by flame photometry and of creatinine (Varley 1954). Blood specimens were taken with minimal stasis from an arm vein with the patient recumbent, and hæmatocrit and serum sodium and potassium were estimated. At times urinary chloride was measured by the standard Volhard titration (King and Wootton 1956). Mostly the ordinary hospital diet was fed, without extra salt at table. During the low-sodium studies, however, a liquid diet (200 g. 'Edosol', Trufood; 80 g. 'Casilan', Glaxo; and 100 g. sucrose whisked gradually into 1200 ml. warm water) was given as six two-hourly feeds in the day. Alternate feeds were supplemented with three pieces of salt-free 'Ryvita' (10 g. per piece) spread with 'Stork' salt-free margarine (30 g. per day), and measured volumes of water flavoured with Rose's sugar-sweetened orange or lemon squashes. Sugar-coated salt tablets were given to vary sodium intake. No drugs (hypnotics, tranquillisers, &c.) were used.

Results

CASE ONE

A clergyman, aged 48, had alternating manic and depressive phases in regular six-weekly cycle for the past

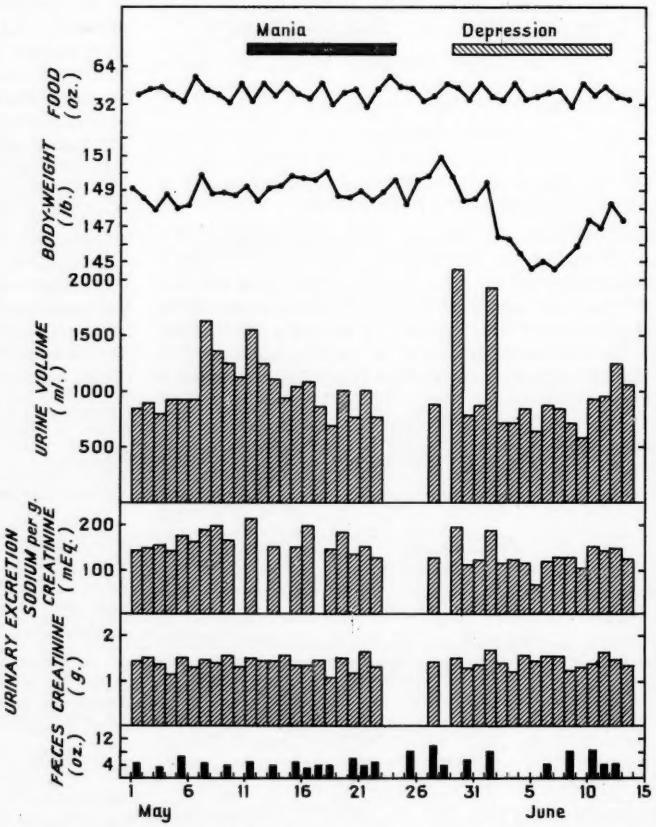

Fig. 1—Case 1: body-weight, food-weight, and daily fæcal excretion charted to the same scale during manic-depressive attack.

Note high twenty-four-hour urine volumes on May 29 and June 1, despite constant daily fluid input (1200 ml.). Entries for fæces are on three times the scale of those for food.

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three years despite various treatments, including chlorpromazine and reserpine (Crammer 1959, case 2). He was kept on weighed hospital diet, and 1200 ml. fluids daily, throughout two cycles. One is shown in fig. 1. Food intake shows only moderate fluctuations, unrelated to mood. Body-weight is fairly constant until the onset of depression when it drops steadily by about 6 lb. in the course of a week. At the same time, twenty-four hour urine volumes rise to their highest values (over 2 litres), and the sodium excretion also rises. When the body-weight begins to recover the urine volume is the lowest of the series, although relative constancy of daily creatinine values points to satisfactory collections. The highest urinary outputs (around 1500 ml.) up to the beginning of the manic phase cannot be explained at present, but they were not associated with a consistent change in body-weight. The relation between depression and fall in body-weight was observed in the next cycle.

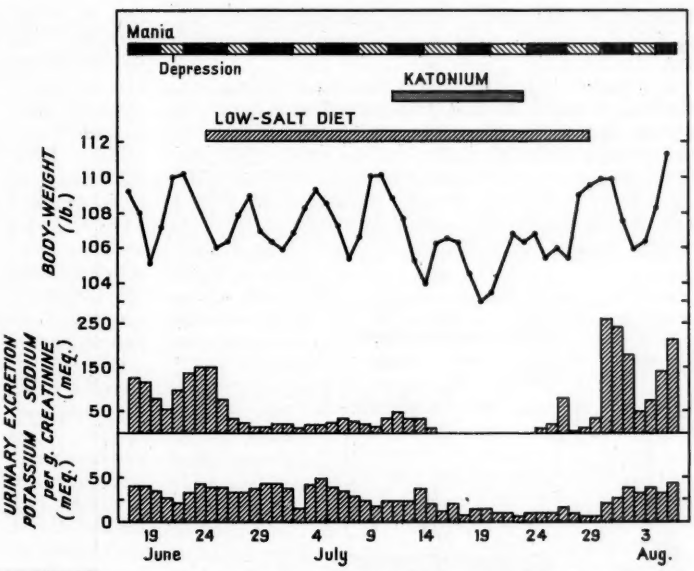

Fig. 3—Case 2: body-weight and sodium excretion on an imperfect low salt diet, with and without katonium, in a general mental ward.

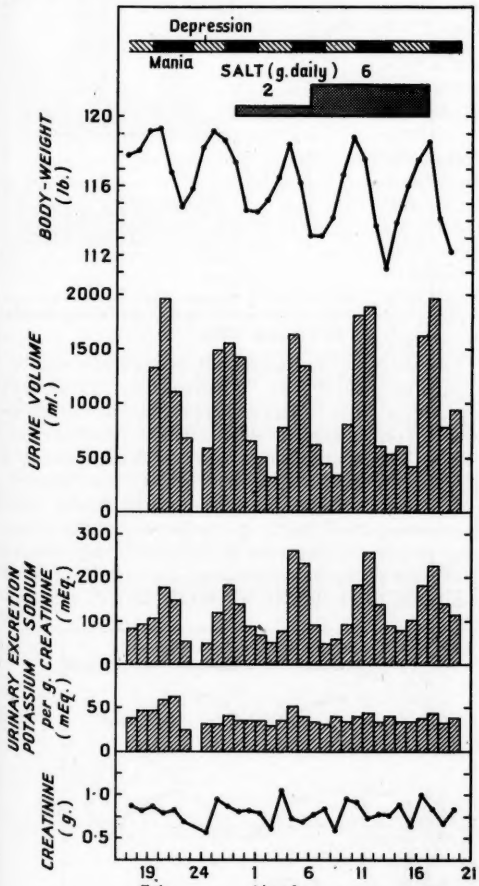

Fig. 2—Case 2: cyclic changes in body-weight, twenty-four-hour urine volume, and urinary sodium on free diet and fluids.
Note steadiness of urinary potassium. Weight loss becomes greater during intake of extra salt (6 g. [100 mEq.] per day).

CASE TWO

A workman, aged 49, had for at least five years, since exact records were kept, suffered a regular six or seven day cycle of symptoms, approximately two days in stupor and four in manic overactivity (Crammer 1959, case 1). When weighed daily while on uncontrolled food and fluid intake he was found to gain weight during the inactive phase and oliguria, and lose it during the onset of the active phase and polyuria (fig. 2). Occasionally polyuria was noted while the weight was still rising (Feb. 24, March 16). During the polyuria extra sodium chloride was lost in the urine, the urinary sodium level increasing threefold from 50 mEq. per litre (in oliguria) to 150 mEq. per litre. Further, the size of the weight loss in each cycle was increased when the dietary intake of sodium chloride was increased (fig. 2), and decreased when foods containing much sodium were excluded from the diet and in addition ' Katonium ' ion-exchange resin (40 g. per day) was given by mouth (fig. 3).

The patient was placed for two weeks on a special low-sodium milk diet (see methods), which was supplemented in the second week by salt tablets 6 g. daily (fig. 4). In the first week, during the inactive phase (Nov. 14–16), the weight gain was small, and no increase in urinary sodium was observed on the first " hypomanic " day (Nov. 17). In the second week the weight gain was over 1 lb. per day (Nov. 20–22), while most of the administered salt did not appear in the urine until the renewed " hypomanic " onset (Nov. 23). Chloride excretion paralleled sodium; while potassium showed little change.

The basal diet yielded about 15 mEq. sodium per day, to which salt tablets added just over 100 mEq. On Nov. 20–22 a total of 345 mEq. sodium was given, and only 28+33+58 (=119) mEq. appeared in the urine. Thus 225 mEq. was unaccounted for. Extracellular fluid contains about 140 mEq. sodium per litre (Elkinton and Danowski 1955), so if all this sodium were retained in

extracellular fluid there would be a net gain of 1600 ml. or 3 lb. 9 oz. weight. The recorded gain in body-weight was 3 lb. 14 oz.

In a further period the effect of fluid intake was studied. On Nov. 26 and 27 the daily fluid was restricted to 500 ml. per day (fig. 5). Although these were inactive days the body-weight remained steady; and the total weight gain in the cycle was smaller than in the cycles before and after, when more water was allowed. Between Nov. 28 and Dec. 5 daily intake was constant at 1600 ml., yet urine volume showed cyclic fluctuation, being biggest (over 1600 ml.) when the body-weight showed greatest decline.

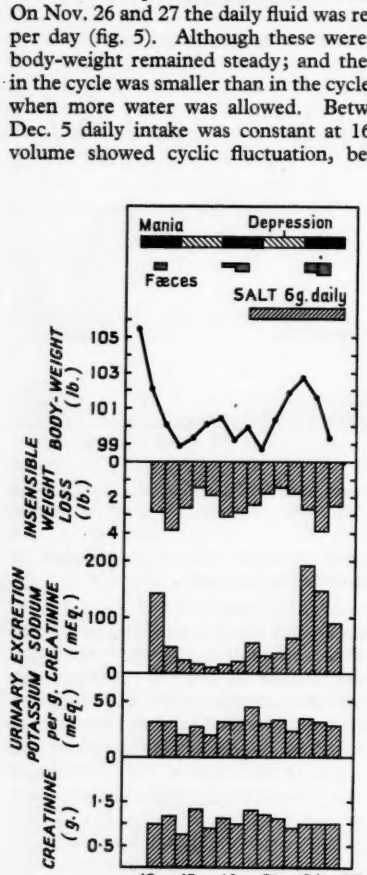

Fig. 4—Case 2: fifteen days on the same daily intake of a low-sodium milk diet, supplemented by 6 g. salt daily in the second week. Insensible weight loss calculated as the daily difference between weight of food in and excreta out and change in body-weight.

Mental Changes

Variations in sodium intake did not alter the mental symptoms. The period of dehydration did not alter the quality or duration of depression. The following overactive phase lasted a day longer, but this sometimes happened also in other cycles.

Blood Changes

Daily estimations of packed-cell volume in normal cycles showed hæmodilution during the inactive phase, reaching a maximum at the onset of polyuria, thus: Nov. 19, 46%; Nov. 21, 42·5%; Nov. 23, 40% (fig. 6). Such a change was not observed during the low-salt diet.

Serum-potassium remained constant. Serum-sodium fluctuated between 135 mEq. per litre and 145 mEq. per litre, reaching the lower value at the onset of polyuria, and running parallel with the degree of hæmodilution. It also fluctuated on the low-sodium diet. Serum sodium and potassium are normally very constant in a given individual (Fawcett and Wynn 1956).

Antidiuretic System

Although the large salt loss in most of the polyuric periods indicated an osmotic rather than a water diuresis, it was possible that fluctuating secretion of antidiuretic hormone might also play a part in the alternating polyuria and oliguria. Vasopressin tannate in oil injections were therefore given (fig. 7). The weight fell much as before, and the sodium loss was as great or greater (urine collection was incomplete, unfortunately). In a subsequent test, aqueous vasopressin intramuscularly, 15 units repeated after four hours, was without effect on the polyuria. The patient smoked most cigarettes (10–15 per day)—i.e., received most antidiuretic stimulation by nicotine—on the day in each cycle when his poluria was greatest.

Effect of Chlorpromazine

Treatment with tablets, 300 mg. daily raised after a week to 450 mg. daily, caused the body-weight to climb steadily; it increased by 12 lb. in sixty days. The weight cycle diminished in amplitude and became rather irregular (fig. 8). When the dose was raised to 900 mg. daily a cyclic variation reappeared, but the amplitude was still only about half what it had been before treatment began. The mental rhythm continued with unchanged period; but the inactive depressive phases were shorter, while the talkative overactivity disappeared almost completely, showing itself chiefly on the last day of the phase, when the patient still muttered to himself. Urine analyses were made for seven days after seven and a half weeks of treatment and for a further seventeen days at the con-

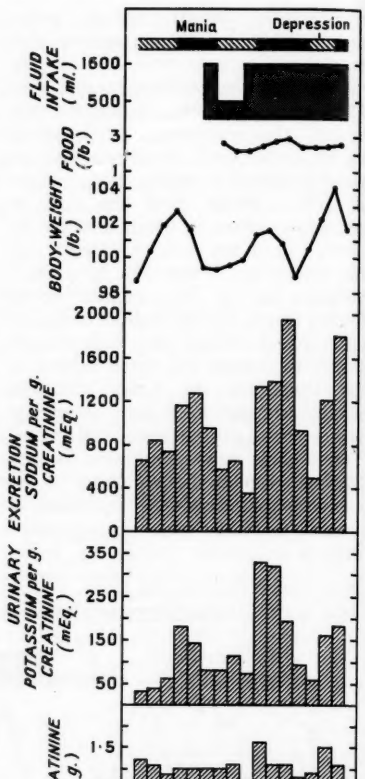

Fig. 5—Case 2: changes in body-weight, twenty-four-hour urine volume, and urinary sodium on constant fluids.

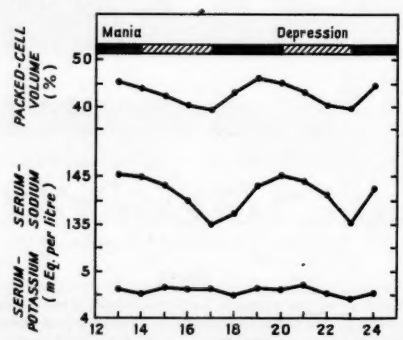

Fig. 6—Case 2: changes in packed-cell volume and serum-sodium.

clusion of treatment (fig. 9). They showed that the peak sodium loss and weight loss now occurred at the start of inactivity, and the weight was regained principally after the active phase returned once more. Blood changes were just detectable: at the time of weight minimum (9 st. 0 lb. 6 oz.) hæmatocrit 42%, serum-sodium 142·5 mEq. per litre, serum-potassium 4·65 mEq. per litre; at a time of weight maximum (9 st. 3 lb.) hæmatocrit 39·6%, serum-sodium 140 mEq. per litre, serum-potassium 4·6 mEq. per litre.

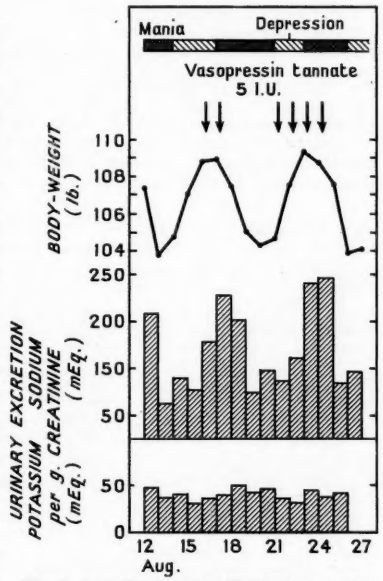

Fig. 7—Case 2: urinary sodium and potassium loss in period of injections of 5 i.u. vasopressin tannate in oil.

Thus there was complete reversal of the relationship previously observed between weight loss and onset of activity: this seemed to begin eleven days after starting treatment (fig. 8). Yet mental and physical rhythms still marched together, though in this new relation (fig. 9).

Discussion

Case 1 shows that body-weight may fall though diet remains roughly constant and activity is decreased. Case 2 shows that increased insensible loss (sweating, &c.) can account for only a fraction of weight loss, and that the sodium and water content of the body can vary and explain the greater part of the weight change. These two cases are far from unique.

Klein and Nunn (1945) studied a patient very like case 2, noting both weight loss and periodic polyuria and salt loss, without, however, linking the phenomena or analysing them further. Gjessing (1953) in his later studies of catatonics observed periodic changes in diuresis and salt excretion, and some of his weight curves show regular changes which are made obscure by the small scale of his charts. Broser (1951) found a patient with recurrent stupor and associated polyuria. Dawson et al. (1956) noted that the extracellular-fluid volume (thiocyanate space) decreased when patients had manic or depressive attacks. Rowntree and Kay (1952) observed fluctuations in serum and urinary sodium while two catatonic patients were on diets. Ström-Olsen and Weil-Malherbe (1958) also observed polyuria during manic phases, and increased sodium excretion in one patient during recurrent manic attacks, but input and output were not well controlled. Pincus and Hoagland (1950) reported statistically significant greater sodium excretions in a group of chronic schizophrenics, while polyuria in such cases has often been seen (Altschule 1953). Disturbances in water and electrolyte metabolism may therefore prove an important feature of mental illness.

Most workers have not appreciated, however, that such biochemical changes may be reflected clinically in changes of body-weight, nor that at one stage of a depressive attack a patient may be losing weight (polyuria), at another stage of the same attack gaining weight (oliguria). It is therefore important in making biochemical studies of patients to define at what stage of their illness they are, and not to be satisfied simply with a clinical diagnosis. Such a definition requires a statement of the directions in which a patient's physical and mental conditions are changing, taken from reference-points given by the clinical history. Body-weight is one such useful parameter. The degree of hydration of the blood may be another, and changes detected in the levels of plasma constituents may be misleading if not corrected for simultaneous changes in blood hydration.

The role of the central nervous system in the control of body-water has been little studied, though salt-wasting and salt-retaining syndromes are already recognised as an occasional consequence of cerebral injury (Welt et al. 1952, Allott 1957). Polyuria can result from hypothalamic disorder, and urine flow and sodium excretion can vary in response to emotion (de Wardener and Miles 1953).

In the second patient chlorpromazine, a drug which acts predominantly on the brain, diminished the cyclic weight swing and altered the timing in the cycle of both mental changes and weight and sodium loss. These facts support the concept of nervous control of body-weight, which might be exerted directly through renal sympa-

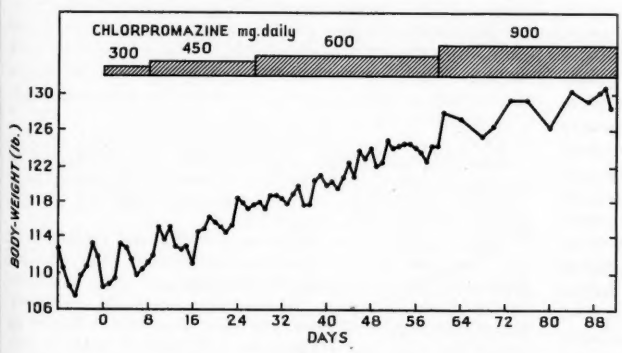

Fig. 8.

Fig. 8—Case 2: body-weight. Double peak at days 10–12 initiates irregularity.

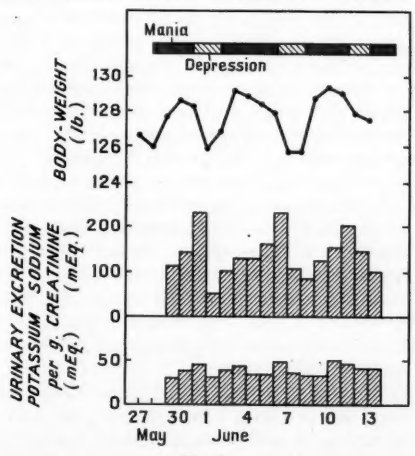

Fig. 9.

Fig. 9—Case 2: daily urinary sodium and potassium excretion after over seven weeks' treatment with chlorpromazine.

thetic nerves, or through pituitary and adrenal hormonal secretions. The fact that daily creatinine excretion varied very little between periods of oliguria and polyuria when urine was very carefully collected (e.g., fig. 4) suggests a fairly steady glomerular filtration-rate. On the other hand, during oliguria both serum-sodium and packed-cell volume fell, indicating interruption of the normal regulation of blood tonicity through the hypothalamic posterior-pituitary system, while the sodium-potassium ratio in the urine also attained its lowest level (around 2) suggesting enhanced adrenal-hormone (aldosterone) secretion in this phase of the cycle. As for the polyuria of the other phase, recent work (Dingman et al. 1958) suggests that sharp rises in cortisol in the blood may produce diuresis and natriuresis, and some measurements of adrenal corticol function which will be reported later are consistent with this idea.

Finally, are the body-fluid disturbances responsible for some of the mental symptoms? Both sodium depletion (McCance 1936) and overhydration (Wynn and Rob 1954) can produce mental symptoms such as lethargy and depression in healthy subjects. Many patients, however, tolerate greater degrees of hyponatræmia than were shown by case 2, without developing mental symptoms (e.g., see Schwartz et al. 1957); nor did dehydration alter this patient's symptoms. Loss of body-fluid was associated with depression in case 1, but heralded hypomania in case 2. With chlorpromazine treatment, however, the relationship between mental and physical symptoms was changed in the second patient, so that loss of body-fluid now went with depression. Clearly there can be no simple connection between the two. It is therefore more likely that here mental and physical signs both result from some deeper process, rather than that one causes the other. At the same time, not least because of Woodbury's (1958) demonstration that changes in cerebral excitability in rats can be induced by changes in steroids and electrolytes, the possibility must remain open that in some patients water and electrolyte disturbances may lie at the root of their illnesses.

Summary

A metabolic study of two chronic psychotic patients with recurring mental disturbances showed periodic losses and gains of body-weight associated with particular phases of the mental illness, while food and fluid intake were steady.

Weight loss was accompanied by polyuria with increased urinary excretion of sodium chloride, weight gain by oliguria and sodium retention. In one patient weight was lost at the beginning of an attack of depression, in the other it began just before emergence from a depressive semistuporose state and the start of a hypomania.

In the second patient, who was studied in greater detail, the weight variation could be almost abolished by decreasing the sodium or water intake, without, however, grossly affecting the mental symptoms. Cyclic fluctuations were demonstrated in serum-sodium and packed-cell volume, relative hyponatræmia and coincident greater hydration of the blood being observed just before the onset of each polyuric phase. Chlorpromazine treatment increased the total body-weight, diminished the weight fluctuation in each cycle, modified the mental symptoms in each cycle without altering the rhythm, and shifted the time of weight and sodium loss to the onset of each depressive phase.

Body-water changes (and hence body-weight changes) may result from the central nervous disturbances occurring in some mental illness, probably through the hypothalamic-endocrine system.

I am deeply grateful to Dr. Joel Elkes for the opportunity to undertake this work, and to Dr. W. Mayer-Gross for his great encouragement and stimulation. Many people helped at different stages: Dr. Victor Wynn; Prof. J. R. Squire and his staff, especially Mrs. Marjorie Harris (dietitian); Prof. K. Kolle (Munich); Dr. J. J. O'Reilly and the medical and nursing staff of All Saints' Hospital, Birmingham, especially Mr. V. G. March (kitchen manager), Mr. W. Blythin (chief male nurse) and Mr. F. Wilks, Mr. J. Greaves, and Mr. M. McCarthy. To them, to Miss Sheila Spanner, and to others unnamed, I tender my thanks.

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DEFECTIVE LACTOSE ABSORPTION CAUSING MALNUTRITION IN INFANCY

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THE cause of failure to thrive in infancy is often hard to determine, and in breast-fed infants whose milk intake is adequate, inability to gain weight, if not associated with any signs of disease, can be particularly puzzling.

This paper records the history of two siblings whose failure to thrive was eventually found to be due to a selective inability to metabolise lactose. As far as we know such a disorder has not previously been reported.

Case-reports

Case 1.—A boy, born April 14, 1949, the second child of healthy parents (the first was a 7-month premature baby who died after 30 hours). Pregnancy and delivery normal, birthweight 8 lb. 6 oz., breast-fed.

At one week the stools became frequent and loose (10–12 per day) and his buttocks excoriated; there was excessive flatulence. He cried a great deal by day and night, and drew up his legs as if in pain. He was taking his feeds ravenously and repeated test weighings over 24-hour periods indicated an intake of 24–30 oz. He appeared completely healthy, and clinical and routine laboratory examination revealed no abnormality. Yet by the end of the 4th week the infant had not regained his birthweight.

The maternal milk was then examined for its protein, fat, and sugar content. While protein and fat were normal, the

lactose content was only 3·5 g. per 100 ml. (normal value 7 g.). The lactose determination was repeated on several occasions on samples obtained at the beginning, middle, and end of feeds, but the results were the same.

In order to increase the carbohydrate intake, 1–2 teaspoonfuls of a cereal in expressed breast milk were given before each feed. Gradually this was increased to 4 teaspoonfuls. From the day the cereal was introduced the baby started gaining weight rapidly and by the age of 3½ months he had doubled his birthweight (fig. 1). Mixed feeding was gradually introduced and by the age of 6 months the infant was weaned. He continued to gain weight rapidly and trebled his birthweight by the age of 9 months. Except for recurrent attacks of tonsillitis and measles he remained in good health. Now, at the age of 10 years, he is a strong, well-developed boy of 4 ft. 6 in. in height, weighing 78 lb.

Case 2.—The sister of case 1, born Dec. 25, 1957. Birthweight 8 lb. 12 oz. Normal pregnancy and delivery, lactation fully established after 5 days. After the initial weight loss the baby's weight remained stationary for 4½ weeks in spite of adequate food intake. The maternal milk was examined on several occasions in two different laboratories and found to be normal. Medical and laboratory investigations were negative.

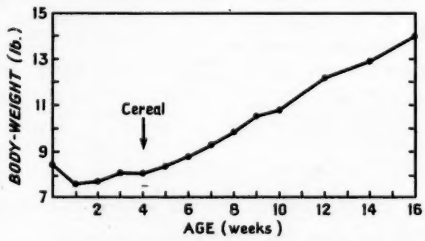

Fig. 1—Weight chart in case 1.

The infant cried frequently as if in pain and passed a great deal of flatus. The motions (8–10 in 24 hours) were loose but of normal colour.

At the age of 4½ weeks 1–2 teaspoonfuls of a cereal were given before each feed, in spite of the normal lactose content of the breast milk. From then onwards the baby's weight increased, though rather slowly (fig. 2).

Complementary feeding with a proprietary brand of half-cream dried milk containing added lactose (milk I) was started at 6½ weeks. As the weight gain still seemed inadequate, a disturbance of lactose utilisation was considered as a possible cause. The proprietary milk preparation was, therefore, replaced by half-cream National dried milk (milk II) with added sucrose, the cereal supplement being maintained. From that day the baby's weight increased rapidly. At the age of 15 months she is in excellent health, her stools are normal, and her weight is 25 lb. She is prone to excessive sweating, as are her older brother and her father.

Special Tests

The initial failure to gain, followed by a rapid increase in weight associated with the addition to the diet of starch or sucrose, suggested that the lactose might not be hydrolysed in the intestine. In order to verify this, lactose and glucose-

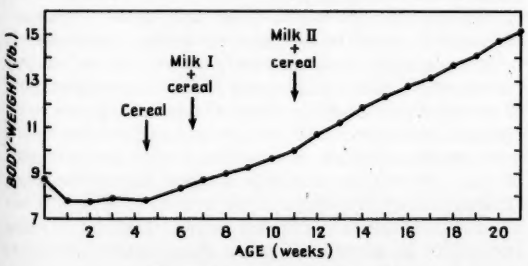

Fig. 2—Weight chart in case 2.

TABLE I—LACTOSE ABSORPTION TESTS IN NORMAL INFANTS AND PATIENTS

3·5 g. lactose per kg. body-weight, up to a maximum of 40 g., was given, in water, by mouth; case 1 and parents received 80 g. Blood-glucose and blood-galactose were determined fasting, ½, 1, 2, and 3 hours after test feed

—	Blood-glucose (mg. per 100 ml.) (galactose in parentheses)				
	Fasting	½ hr.	1 hr.	2 hr.	3 hr.
Normal infants					
1	81 (0)	112 (43)	112 (11)	112 (0)	85 (0)
2	58 (0)	74 (30)	116 (0)	162 (0)	132 (0)
3	70 (0)	101 (0)	140 (20)	124 (0)	101 (0)
4	81 (0)	159 (0)	143 (16)	..	..
Patients' parents					
Father ..	104 (0)	151 (0)	159 (25)	..	..
Mother ..	108 (0)	139 (19)	87 (11)	..	..
Patients					
Case 1 ..	66 (0)	74 (0)	81* (0)	70 (0)	70 (0)
Case 2 ..	78 (0)	85 (0)	81 (0)	70 (0)	78 (0)

* Ate a sweet before 1 hr. reading.

plus-galactose absorption tests were performed. The boy was given 80 g. of lactose on one occasion and 40 g. each of glucose and galactose on another, while the baby received half that dose. Blood glucose and galactose were determined, testing at ½, 1, 2, and 3 hours after administration of sugar. Lactose-absorption tests were also carried out on 4 normal infants (tables I and II) and on the patients' parents.

The results of these tests showed quite definitely that glucose and galactose were readily absorbed in both siblings, but that ingestion of lactose did not lead to any significant increase in the blood-level of monosaccharides which was observed in normal individuals. The parents also had a normal lactose absorption.

A determination of fæcal fat in the younger sibling gave a value of 10%, indicating that there was no impairment of fat absorption. Bacterial examination of the fæcal flora revealed no gross abnormality. No lactose was found in the fæces.

Discussion

The weight charts and the sugar-absorption tests show clearly that the two siblings are unable to metabolise lactose. Since this disaccharide is not normally absorbed as such but is hydrolysed into its component hexoses by intestinal lactase, it is reasonable to infer that the specific

TABLE II—GLUCOSE + GALACTOSE ABSORPTION TESTS

Case 1: 40 g. each of glucose + galactose. Case 2: 20 g. of each sugar

Case	Blood-glucose (mg. per 100 ml.) (galactose in parentheses)			
	Fasting	½ hr.	1 hr.	2 hr.
1	58 (0)	88 (0)	102 (29)	132 (12)
2	78 (0)	102 (24)	125 (24)	..

lesion is a failure to hydrolyse lactose. This may be due to an actual deficiency of lactase, or to inhibition (or lack of activation) of the enzyme.

The large number of stools, flatulence, and colic might well be due to increased fermentative breakdown of lactose by intestinal bacteria resulting from the non-absorption of the disaccharide. It is to be expected, therefore, that none of the sugar would appear in the fæces.

Considering that lactose is the only carbohydrate present in any quantity in milk and constitutes normally about 40% of the total calorific value, it is not surprising that an inability to utilise this sugar results in a failure to gain weight. In these circumstances the blood-glucose level could be maintained only by gluconeogenesis—i.e., by the deamination of dietary or endogenous aminoacids, which might be expected to lead to an increased urea excretion.

The inability to hydrolyse lactose, even if compensated for by the addition of starch or sugar to the diet, means

that the infant is deprived of galactose. As it is not yet known whether dietary galactose plays any vital part in the nutrition of the young, the younger sibling is now being given an appropriate dose of this monosaccharide. The excellent state of health of the 10-year-old boy, however, suggests that at least up to this age absence of dietary galactose does no detectable harm.

The presence of this enzyme defect in two siblings suggests that the condition is hereditary. If this should be confirmed, the normal lactose absorption in the parents would exclude dominant transmission of the trait. The hereditary aspects, as well as some biochemical features of the disorder, are now being studied. Should absence of lactase be demonstrated, " hereditary alactasia " seems to be an appropriate name. We do not know yet whether the peculiar abnormality of the mother's milk, which we observed during the lactation of the older sibling, is in any way connected with the enzyme deficiency in the children.

Summary

A hitherto unrecognised congenital abnormality is described which consists in the inability to hydrolyse lactose. It manifests itself in a failure to gain weight in spite of adequate food intake, an increased number of stools, flatulence, and colic.

Inability to hydrolyse lactose can be demonstrated by means of lactose and glucose-plus-galactose absorption tests, and can be compensated by addition of non-lactose carbohydrate to the diet. In this way an adequate calorie intake is achieved which results in an immediate gain in weight. The provision of dietary galactose may be desirable.

The condition has been observed in two siblings, thus suggesting that it may be inherited. Since the failure to gain weight is due to lack of utilisable carbohydrate it is more likely to become obvious in breast-fed infants than in babies receiving dried-milk preparations which contain sucrose or glucose.

Preliminary Communication

ISOANTIBODY FORMATION IN CHRONIC PANCREATIC DISEASE

THE demonstration that experimental pancreatitis could be produced readily by means of various sensitisation reactions [1 2] and the current interest in " autoimmune " phenomena [3] have prompted us to determine the possible development of specific pancreatic antibodies in experimental and clinical pancreatitis.

Pancreatic antigen was prepared by saline extraction of ground pancreas from several dogs. Normal dog and human sera showed no precipitin reaction to this antigen. However, in dogs with experimentally produced pancreatic necrosis precipitins were demonstrable within 9–18 days. Similar results were obtained in rabbits.

TABLE I—RESULTS OF PRECIPITIN TEST

Groups	No. of cases	No. with positive test
Chronic pancreatitis	17	16
Carcinoma of pancreas	5	4
Cystic fibrosis of pancreas	1	1
Unselected hospital patients	147	4
Blood donors	50	0
Selected controls:		
Disseminated lupus erythematosus	3	1
Hypergammaglobulinæmia	3	0
Rheumatoid arthritis *	6	0
Total	232	26

* Cases with positive latex-fixation tests.

Rabbits that had been immunised against pooled homologous pancreas in Freund's adjuvant demonstrated precipitins to the antigen within 12–14 days. The antibodies appeared to be both species and organ specific since there were no demonstrable precipitins against homologous liver, kidney, lung, and spleen antigens or against heterologous pancreas antigens.

A clinical study was then made by titrating human sera against antigens made from human pancreas obtained at necropsy. Five groups of patients were studied: (*a*) patients with chronic pancreatitis proven at operation; (*b*) patients selected because of known chronic pancreatic disease other than chronic pancreatitis; (*c*) unselected medical and surgical hospital patients; (*d*) healthy blood-bank donors; (*e*) selected group of patients with diseases in which specific and non-specific antibodies have been described.

TABLE II—ANALYSIS OF POSITIVE REACTIONS IN OTHER DISEASES

Diagnosis	Precipitin reactions with homologous antigens			
	Pooled pancreas	Liver	Kidney	Spleen
Disseminated lupus erythematosus	+	+	+	+
Chronic glomerulonephritis	+	−	+	−
Chronic ulcerative colitis	+	−	−	−
Chronic cholecystitis	+	−	−	−
Diabetes mellitus	+	−	−	−

The results of the study are summarised in table I 26 of the 232 sera examined gave a positive precipitin reaction. 16 of the positive sera were from patients with proven chronic pancreatitis. 4 patients with known carcinoma of the pancreas and 1 patient with cystic fibrosis of the pancreas showed precipitins. 1 patient with two documented attacks of acute pancreatitis and 1 with known carcinoma of the pancreas failed to give a positive reaction. Of the remaining 211 patients, 5 were positive. The primary diagnoses of these 5 patients are shown in table II.

The antibodies found in the human sera appeared to be both organ and species specific except in the cases of (*a*) a patient with disseminated lupus erythematosus who reacted with all homologous antigens and (*b*) patient with glomerulonephritis who showed, in addition, precipitins to kidney antigen. In the patients with chronic pancreatic disease the antibody to the pancreatic antigen could not be adsorbed with homologous liver. This finding suggests that the antibody is organ-specific and is formed as a result of the liberation of a pancreatic antigen regardless of the nature of the underlying disease.

1 patient (case A) whose serum contained a high antibody titre to pooled human pancreas antigen, subsequently underwent distal pancreatectomy on account of chronic pancreatitis. This circumstance provided an opportunity to see whether case A's serum contained precipitins to an antigen derived from his own pancreas. No precipitins were shown, although the sera from other patients with chronic pancreatitis regularly showed precipitins when titrated against A antigen. This finding agreed with our experimental studies in which animals exposed to their own pancreas, altered by trauma or adjuvants, produced antibodies reacting in vitro to homologous but not to

1. Thal, A. P., Brackney, E. *J. Amer. med. Ass.* 1954, **155**, 569.
2. Thal, A. P. *Surgery*, 1955, **37**, 911.
3. Doniach, D., Roitt, M. *J. Clin. Endocrin.* 1957, **17**, 1293.

isologous pancreatic antigens. At present, this antibody should be called an isoantibody rather than an auto-antibody. A broad explanation of such results has been put forward by McKay et al.,[4] who has suggested two possibilities:

(*a*) An inhibitory substance is present in tissue extract or serum of the individual which blocks the precipitin reaction in vitro.

(*b*) The tissue extracts lack determinants capable of reacting with the serum of the same individual. In this instance McKay has suggested that the individual-specific antibodies are rapidly adsorbed on to the specific organ, leaving only the species-specific antibodies to react with antigens derived from other individuals.

If a hypothetical inhibitory substance prevents union of antibody and antigen in the individual, it is conceivable that fluctuations in the intensity of the inhibitory reaction might account for the acute and chronic exacerbations in pancreatitis. While the precise role of these antibodies in influencing the course of pancreatic inflammatory disease is unknown, it is nevertheless apparent that this precipitin test may be of considerable value in diagnosis.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Problems of Irradiation in Childhood

THE Section of Pædiatrics met on May 22, with the president, Dr. CHARLES PINCKNEY, in the chair, to discuss this subject.

Prof. DOUGLAS HUBBLE thought that pædiatricians should accept the probability that children were especially sensitive to the effects of radiation—less sensitive than the fœtus but more sensitive than the adult—and that therapeutic radiation in children should be used only for malignant disease. The Ministry of Health report recommended that miniature radiography was unsuitable for children because there was, by this method, a proportionately greater surface irradiation of the child than the adult. The prophylactic and therapeutic advantage of miniature radiography for the mass of children was negligible, and this method should be excluded even if the radiation dose were less than it was.

A straight chest X-ray in a 6-year-old child should deliver a dose no higher than 0·015r, while screening under the best conditions would give a dose of 0·7r per min. for an average time of 2 minutes—an exposure about 100 times as great. And cardiac catheterisation, taking a maximum time of 20 minutes, would provide an exposure 1000 times as great as a single chest X-ray. Pædiatricians must realise that an intravenous pyelogram in a baby might *trigger off* leukæmia in a child with a predisposition—a possibility that called for caution but not alarm. The self-questioning imposed by the recently recognised radiological risks would improve medical practice, medical education, and medical ethics.

Turning to the use of isotopes, Professor Hubble said it was customary to assume that isotopes with a short half-life might safely be used in children. ^{24}Na had a half-life of only 15 hours, and this isotope was often used to localise the placental site. What evidence was there that this method was less harmful either to the fœtus or to the mother's gonads than a diagnostic X-ray? And had the mothers and children concerned in these investigations been adequately followed up? In the investigation of thyroid disease in childhood, the iodine isotope with the short half-life, ^{132}I (2·3 hours), should be used rather than ^{131}I (8 days). ^{132}I was suitable only for short uptake studies, and there were many better methods for the diagnosis of both hypothyroidism and hyperthyroidism in children. This isotope was in fact useful only for localising the site of the thyroid gland which had imperfectly descended.

For those who believed, as Professor Hubble did, that the experimental method must be used in man, the use of isotopes in children for the investigation of disease raised ethical difficulties. Could we be sure that, with the use of isotopes of short half-life and in tracer doses, there was no risk—or, at least, that the risk was no greater than that of other widely used diagnostic procedures?

Describing the X-ray histories of 1299 healthy children and 1299 children who died of malignant disease before the age of 10 in 1953–55, Dr. ALICE STEWART said that the number of children who had been X-rayed after birth but before the onset of the fatal illness was almost equal to the number of healthy children who had been X-rayed in the equivalent period. But twice as many of the children who died had been X-rayed within a year of birth. Hence the excess of first-year X-rays among those who died was balanced by a deficit of other postnatal X-rays. For children who died of leukæmia between two and four years of age, however, there was a significant excess for all postnatal X-rays.

In the absence of an overall excess of postnatal X-rays among those who died there was no evidence that such X-rays increased the number of deaths from malignant disease before the age of 10. They may, however, have altered the age-distribution of deaths in childhood from leukæmia. The high proportion of X-rayed children who died of leukæmia between 2 and 4 years of age would be explained if X-rays in infancy hastened the onset of leukæmia in children already predisposed to it. This would also explain why the children who died of leukæmia between 5 and 10 had had slightly fewer X-rays than the corresponding control children. Only 11 children in both groups had been given radiotherapy, all of whom were girls treated for nævi. They included 3 of the control group, 5 who died of leukæmia, and 3 who died of other malignant diseases. In the same groups of children, the numbers who had been X-rayed in utero were approximately twice as great among those who died as among the control children.

Prof. G. M. WILSON said that therapy doses of radio-isotopes for children could hardly ever be justified. Certainly radio-iodine should not be used for the treatment of thyrotoxicosis in young people. It might be used in a few cases of thyroid carcinoma with metastases that could not be treated surgically. Discussing tracer doses in diagnosis, Professor Wilson said that in several tests the isotope was widely dispersed in the body and irradiation was fairly uniformly distributed. Radio-iodine, however, was concentrated in the thyroid, which consequently received a high dose, and there was considerable evidence that in childhood the thyroid was more sensitive to the carcinogenic effect of ionising radiation. In a group of children who had had cutaneous lesions of the neck

4. McKay, I. R., Larkin, L., Burnet, F. M. *ibid.* 1957, ii, 122.

treated by radium or X rays and in whom the thyroid was exposed, the dose had sometimes been large, but in others it had been small, less than 200r. The latent period also varied greatly. It was not always apparent that a carcinoma was related to irradiation in childhood: in 1 patient, who had ringworm of the scalp which was over-irradiated when she was 5 years old, a thyroid cancer developed 35 years later. These dangers were now widely recognised.

The interpretation of radioisotope tests might be difficult, since normal values in healthy children would not be available and it would be quite unjustifiable to expose them to irradiation. Most radioisotopes, even in adults, were still used chiefly for the investigation of disease rather than for the diagnosis of individual cases. Concerning a particular patient, the clinician must decide, balancing the hazards against the benefit to the patient, and recourse to radioisotopes in children would only rarely be indicated.

Dr. C. O. CARTER said there was no direct evidence of radiation-induced mutation in man, but it could be taken for granted that such mutation occurred, though the size of its effects was known with much less certainty. Chromosome mutations and mutant genes were now perhaps responsible directly for about 1 in 6 of infant deaths, while indirectly, associated with environmental factors, mutant genes probably accounted for more than another 1 in 3. Together then, chromosome mutations and mutant genes probably accounted for more than half the infant deaths in this country.

In trying to assess the radiation dose required to double the mutation-rate, it was the average dose to the gonads of the population as a whole that was important. A large dose to a few individuals was relatively unimportant, since even if the risk of having a child affected by a fresh mutation was doubled, that risk was still a small one. It was thought until recently that it did not matter whether the dose was given at low intensity over a long period or high intensity over a short period, so that the doubling dose of artificial radiation could not be less than the natural background radiation, which in this country averaged about 3r over 30 years. Recently, however, animal experiments suggested that intensity was important, so that 3r from X rays might cause more mutation than the low-intensity background radiation. But failure to find evidence of an increased mutation-rate in the children of survivors of the atomic bombs in Japan had been taken to indicate that the doubling dose was probably not less than 10r. Experiments on mice indicated that, for some gene loci at least, the doubling dose was about 50r. Sensitivity in man might be more or less than in the mouse, but there was no reason at the moment to suppose that 3r of artificial radiation, mainly from diagnostic X-rays, would add more than about a tenth to the mortality in childhood determined by gene mutations, and probably less.

Reviews of Books

Clinical Neurophysiology

JOHN MARSHALL, M.D., F.R.C.P.E., M.R.C.P., reader in clinical neurology, University of London, and physician, National Hospital for Nervous Diseases, London. Oxford: Blackwell Scientific Publications. 1959. Pp. 296. 37*s*. 6*d*.

NEUROLOGY lends itself more than most clinical subjects to interpretation in terms of its basic science, so that textbooks of neurophysiology can be of direct interest and relevance to the neurological clinician. Fulton's *Physiology of the Nervous System* has been a stand-by for many years, and more recently a new text by E. G. Walsh has provided a more up-to-date and more clinical presentation. Here Dr. Marshall has gone a stage further and produced a book specifically on clinical neurophysiology, thus allowing himself to select what he thinks of special clinical importance.

The book follows a broadly anatomical plan. Early chapters are devoted to the nerve impulse, the neuromuscular junction, and the sensory receptors, and in each the clinical implications are considered. Reflex action, synaptic conduction, and the physiology of the isolated spinal cord are then considered. Later chapters review the brainstem, cerebellum, and thalamocortical system in relation to clinical syndromes. The book is short, so these chapters, which deal with a large and expanding area tend to be compressed and incomplete. The early ones, however, give a clear and fairly comprehensive survey, which will commend the book both to neurologists and to final-year students.

Vascular Surgery

GEZA DE TAKATS, M.D., M.S., F.A.C.S., clinical professor of surgery, University of Illinois College of Medicine. Philadelphia and London: W. B. Saunders. 1959. Pp. 726. 122*s*. 6*d*.

THIS book reflects the forceful personality of its author, for it is a lucid and persuasive statement of his own decided views on a rapidly expanding territory of surgery. Much of the text is concerned with his own work on experimental or clinical vascular problems: at the same time, other viewpoints are presented and European contributions are not neglected. He first discusses the fundamental principles of hæmodynamics, the physics of shunts, vasomotor control, and blood-clotting: the following chapters are concerned with diagnosis, so leading to the various vascular syndromes. These syndromes are excellently reviewed with relevant case-histories or reminiscences, and Dr. de Takats is not ashamed to admit the limitations of present-day concepts and therapies. The weakest part of the book is the section on surgical technique, which does not contain the detail an occasional vascular surgeon would need. Nevertheless, we welcome Dr. de Takats' contribution as probably the most stimulating, instructive, and entertaining monograph on vascular surgery for many years.

A Manual of Anæsthetic Techniques (2nd ed. Bristol: John Wright. 1959. Pp. 240. 27*s*. 6*d*.).—There are few alterations in the new edition of this essentially practical book by Dr. W. J. Pryor, which will continue to help doctors learning about anæsthesia. A flaw which might be amended in the next revision is the repeated use of trade names of drugs.

Pharmacology (London: Oxford University Press. 1959. Pp. 587. 42*s*.).—Written essentially from the viewpoint of an experimental pharmacologist, Dr. J. H. Gaddum's well-known book has for long proved an excellent bridge from physiological studies to clinical therapeutics. Several new sections have been added, and the discussion of methods used for the study of drugs acting on the brain is particularly noteworthy. The book has been brought completely up to date, and, in spite of the great advances in pharmacology and the enormous number of drugs introduced since the last edition, the increase in size is slight. Though there have been many alterations, the character of the book is unchanged. Many readers will welcome the retention of the valuable key to chemical names, which must greatly help students and many others more remote from their chemistry days to understand the many variants of new drugs. Dr. Gaddum's intention nineteen years ago was that his book should provide for the doctor knowledge of the kind of evidence that justified the trial of new drugs on patients; and this purpose, never more important, has been admirably achieved.

THE LANCET

LONDON 30 MAY 1959

Profession and Public

IN a letter that appears in this issue, Mr. CYRIL BEACH says that the litigant contemplating an action for medical maltreatment may sometimes be impeded by refusal of help, or even by deterrence, from other doctors; and he contrasts this with the willingness of solicitors and other professional people to offer dispassionate advice where the conduct of their own colleagues is in question. Not all may go so far as Mr. BEACH in his assertion that "there is a cloak of conspiracy round the whole profession"; but beyond doubt, when a doctor is under attack by laymen, his colleagues' first reaction is to close ranks round him.

For this there are several reasons—some rational, some less so. Most doctors are proud of their profession and are eager to defend it from onslaught from whatever quarter. The doctor may be mindful, too, that many lay people believe that, if something has gone wrong, someone must be culpable, and he may suspect that only his peers are fit to adjudicate. Furthermore, in the sure knowledge that no-one is a really good doctor all the time, he may be swayed by a feeling that the trouble that has befallen a colleague may, for all he knows, be his own tomorrow. At the same time these motives, though understandable, do not warrant the withholding of the information that Mr. BEACH says should be freely given. Even half a century ago medical knowledge was so pathetically small that, in dealing with patients and the larger public, the need for a barrier of silence to preserve medical status was keenly felt; and usually, no doubt, this barrier benefited the public which, ignorant of how little lay beyond, was confident in its doctors. Nowadays, however, we need not fear to show our hand, whether in consultation, in educating the lay public in medical matters, or in appearing in the courts. As to any misgivings about the courts' capacity to adjudicate fairly, we have to recognise that on the whole these are unsupported by the outcome of cases, that the accepted definition of professional negligence allows a reasonable margin for human fallibility,[1] and that in any event we are not entitled to hamper anyone's recourse to a civil action. Though naturally reluctant to jeopardise a fellow doctor, we are no more entitled to be influenced by this sentiment than is a jury to discharge a careless car-driver because of a lurking fear that one day they, in turn, may be in the dock on a similar charge.

Yet, when all this has been said, we cannot agree with Mr. BEACH that doctors should aid litigants as freely as do fellow-members of other professions. In the first place, most of the actions that bring doctors into court to defend themselves neither are criminal nor arise from wilful negligence: usually they spring from inexperience or an error of judgment; and in such cases caution in expressing an opinion that may tilt the case one way or the other is proper. Secondly, at least in hospitals, these are the days of the medical team; and any one member of the team may not wish, unless compelled, to provide evidence on the action of another member for two distinct reasons: that he values the integrity of the team, which might be shattered if he gave evidence except sub pœna; and that he may himself feel partly responsible for the action in question.

Can there, then, be a middle way whereby the profession can be freed from the suspicion of undue secrecy to which Mr. BEACH has given voice? We believe that there can. One course would be to establish in each region a small advisory committee of, say, three members: one might be appointed by the Royal Colleges and one by the College of General Practitioners; and they would sit under the chairmanship of a layman with legal training. This committee, which would have no mandatory powers and no link with statutory bodies, would have two main functions: first to advise doctors on any help they should give litigants in proposed civil actions (in the light, perhaps, of the opinions of the doctor's defence organisation, which might be represented); and secondly to advise doctors on action where they have noted that a colleague is no longer fit for his professional work. By establishing collective responsibility in some such way as this, we may ensure that members of the public gain any information to which they are entitled before a case comes to court; and willingness to recommend the resignation of an unfit doctor may be increased. These two duties, however unwelcome, cannot honestly be evaded; and responsibility for the second is already under public scrutiny.

1. See *Lancet*, 1955, i, 400

Gastric Ulcer and the Ulcer Equation

WHEREAS the Top People have a duodenal ulcer, gastric ulcer has been regarded in Western Europe for the past half-century as an affliction of the materially and mentally underprivileged. When it has caught the medical limelight it has usually done so either as the disputed parent of carcinoma of the stomach or as a poor relation of duodenal ulcer. The link with duodenal ulcer is examined in two articles in this issue. Dr. AAGAARD and his colleagues (p. 1111) review 313 cases of gastric ulcer. They report that in 30% of patients the gastric lesion was preceded by a duodenal ulcer; and they hint that a more painstaking clinical history, examination, and scrutiny of operation specimens might have revealed a duodenal lesion in an even higher proportion of patients with gastric ulcer. They raise the question whether "secondary" gastric ulceration should not be regarded as the rule rather than the exception—a view which is both directly and indirectly supported by the findings of Dr. MARKS and Professor SHAY (p. 1107). The two groups of workers agree that duodenal ulcer is hardly ever preceded by gastric ulcer.

JOHNSON,[1 2] who repeatedly drew attention to combined gastric and duodenal ulceration, pointed to one of the main reasons why many still find the comparative commonness of this combination difficult to accept. Most of us have been taught that "different sorts of people are attacked by the two lesions"[1]—indeed, so eloquently is the distinction expounded that at times the two groups of patients seem almost at opposite poles in physical and mental constitution. Have these differences been exaggerated; or are we witnessing another of those sudden twists in the natural history of peptic ulcer which have so often confounded those who believe that at last they have understood it? In this particular instance we can perhaps dismiss the second possibility. Though surprisingly little interest was aroused by his findings, the late Sir DAVID WILKIE showed, as long ago as 1926, that combined ulceration is by no means rare: in a series of 300 personal cases he found this combination in no less than 53% of his gastric-ulcer and 16% of his duodenal-ulcer patients.[3] It is more probable that in contrasting the gastric-ulcer and the duodenal-ulcer personality generations of clinical teachers have been their unwitting cartoonists, transforming humdrum reality into images both more and less real. Nobody would deny that the "typical" gastric-ulcer patient differs from the "typical" duodenal-ulcer patient; but the depth of the division is hard to judge. Between the duodenal-ulcer and gastric-ulcer age lies DANTE's "midway" of the human life; and not only different ages but also different kinds of ulcer (and indeed different diseases in general) affect different temperaments differently. The precipitating causes of peptic ulceration are probably as varied as the precipitating causes of traffic accidents; but there is much statistical and experimental evidence to support the suggestion by Dr. MARKS and Professor SHAY that the underlying causes of gastric and duodenal ulcer are very similar. This ætiology they express in the form of an "inescapable equation"—acid aggression *versus* mucosal defence.

Anyone seeking in a court of law to prove "acid aggression" responsible for peptic ulceration would be dismissed after two minutes' cross-examination with a stern admonition not to waste the court's time. But on the unjudicial assumption of guilt until innocence is proved, the hypothesis has served doctors and their patients extraordinarily well. The Acid Saga goes back to the last decades of the 19th century.[4 5] Since then gastric acidity has been studied in immense detail; and it has become the basis of most diagnostic tests and all forms of treatment of ulcers. Misconceptions have taken root as firmly as observed facts. Thus terms such as "achlorhydria" and "anacidity" (coined several years before "pH" was first heard of[4–8]) still mean to most doctors exactly what they meant fifty years ago; and this is the source of a good deal of misunderstanding. Until recently patients were said to have "achlorhydria" or "anacidity" if their gastric juice failed to change the colour of Töpfer's reagent, despite the fact that this reaction takes place at a pH of about 3–4—a hydrogen-ion concentration that would make any other body-fluid (urine, for example) strongly acid. True achlorhydria is extremely rare; and quite severe hypochlorhydria (*çi-devant* achlorhydria or anacidity) can change almost from one day to the next.[9 10] It is in this light that published data of the past must be interpreted: not only occasional case-reports of peptic ulceration in the presence of alleged complete achlorhydria,[11] but even classifications of ulcers according to whether they are associated with "high" or "low" acidity. Despite such misconceptions, we can at least try to translate "acid aggression" from literary into physiological terms. By increasing the dose of histamine while neutralising its systemic effects by anti-histamine drugs, KAY, HUNT, and others have shown that the amount of acid secreted by the gastric mucosa can be increased to about four times the "normal" histamine response[12 13]; but that any further increase in the dose of histamine produces no further rise in the flow of acid. This maximal histamine response moreover, varies with the size of the "parietal (acid-secreting) cell-mass" of the stomach.[14 15] Applied to the ulcer equation, this means that "acid aggression" depends neither on the hyperactivity or hypersensitivity of the acid-secreting cells, nor on any abnormal stimuli, but on the presence of an unduly large number of cells ready to respond to stimulation. This view is supported by the post-mortem studies of Cox,[16] who showed that patients with duodenal ulcer have larger stomachs and more parietal cells, and by clinical investigations involving the maximal histamine response and similar tests.[16–18]

To point to a genetically determined and seemingly slight anatomical variation as the underlying cause of peptic ulceration may offend those who insist that "hydrochloric acid is part of the natural mechanism of protein digestion, and Nature seldom makes mistakes—never stupid ones."[19] But possibly the overgrowth of the parietal cell-mass is not an inborn error at all but a work hyperplasia caused by long-continued nervous or dietetic overstimulation. It is more important to bear in mind that the experimental foundations of such concepts are extremely artificial. Not only are we still unconvinced that histamine is the only final transmitter of gastric secretory stimuli, but the maximal histamine response can be elicited only under pharmacological conditions which have not the

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2. Johnson, H. D. *Surg. Gynec. Obstet.* 1956, **102**, 287.
3. Wilkie, D. P. D. *Brit. med. J.* 1926, ii, 469.
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10. Palmer, W. L., Nutter, P. B. *ibid.* 1940, **65**, 499.
11. Sacks, I. *S. Afr. med. J.* 1954, **28**, 946.
12. Kay, A. W. *Brit. med. J.* 1953, ii, 77.
13. Hunt, J. N., Kay, A. W. *ibid.* 1954, ii, 1444.
14. Hanson, M. D., Grossman, M. I., Ivy, A. C. *Amer. J. Physiol.* 1948, **153**, 242.
15. Adam, H. M., Card, W. I., Riddell, M. J., Roberts, M., Strong, J. A. Woolf, B. *Brit. J. Pharmacol.* 1954, **9**, 329.
16. Cox, A. J. *Arch. Path.* 1952, **54**, 407.
17. Tongen, I. A. *Surgery*, 1950, **28**, 1009.
18. Avery Jones, F. *Brit. med. J.* 1957, i, 719.
19. Ogilvie, Sir H. *Lancet*, 1953, i, 555.

remotest physiological counterpart. Nevertheless, " acid aggression " has now been firmly established as a physiological reality, closely (if not necessarily causally) linked with peptic ulceration; and if this seems a modest claim, it is more than can be made for the other side of the ulcer equation.

Though we talk of " defence mechanisms " which protect us from peptic ulcers, we are far from being able to substantiate any such mechanism with factual data: indeed, many of those put forward seem a priori to be unlikely. Thus to suggest that at an energy expenditure which requires 25 litres of blood per hour the stomach elaborates a concentrated caustic only to have it " neutralised " by fitfully regurgitated intestinal fluid is to accuse nature of most unnatural wastefulness; and it is certainly not a device employed either in man or in dog to combat " acid aggression."[20-22] Food undoubtedly acts not only as a stimulant but also as a substrate, a buffer, and a diluent—and the importance of diet in the treatment of established ulcer hardly needs emphasis—peptic ulcers are probably no more caused by irregular meals than healed by six small meals a day. An exchange-diffusion of sodium and hydrogen ions between blood and stomach contents, with the gastric mucosa acting as a kind of dialysing membrane, certainly helps to regulate intragastric acidity [23 24]; but if this movement of ions is under the influence of any factors other than physical, we have not yet discovered them. (Such factors may none the less exist; and that they play a part somewhat analogous to the adrenocortical and pituitary hormones in tubular reabsorption is a distinct and exciting possibility.) It is when we come to the most obvious line of mucosal defence, however—gastric mucin itself—that hard facts are hardest to find. We know that " mucin " is elaborated by at least three different types of cell and that it is a mixture of mucopolysaccharides (some of which are chemically related to blood-group antigens) and of mucoproteins. They can be divided into " visible mucous ", the sticky, jelly-like coating of the mucosa which is secreted by the surface epithelial cells; and " glandular mucoprotein ", a soluble substance related in some way (perhaps even identical with) Castle's intrinsic factor.[25 26] The secretion of " glandular mucoprotein ", like that of acid, is under the combined influence of nervous and humoral stimuli; but vagal stimulation of mucoprotein secretion, unlike that of acid secretion, does not seem to require an intermediary gastrin-like hormone. Beyond the effect of direct mechanical stimulation, the mechanism of " visible mucus " secretion is unknown: and though it apparently inhibits pepsin and acid and adsorbs histamine and pepsin, whether these functions are of any practical importance in warding off " acid aggression " is uncertain.[27-29] We cannot say, in fact, what defeats the aggressiveness of acid in most people for most of their lives—or, indeed whether it needs defeating at all.

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26. Grasbeek, R. *Acta med. scand.* 1956, Suppl. 314.
27. Glass, G. B. J., Boyd, L. J. *Gastroenterology*, 1953, **23**, 636.
28. Blackburn, C. M., Code, C. F. *J. nat. Cancer Inst.* 1949, **10**, 337.
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Hormone Dependence and Breast Cancer

BECAUSE many further patients have been hypophysectomised on account of breast cancer, knowledge of pituitary-endocrine relations has been extended in the past two years [1]; but little progress has been made towards deciding whether any breast carcinomas are permanently dependent on the hormonal conditions in which they came into being. Hypophysectomy has continued to be a last resort for metastatic breast cancer; and in recent reports remission-rates and survival-times remain substantially unchanged. Of 218 of these very ill patients in two groups, altogether 16 died within thirty days after operation; but in the second group of 109, death was attributed to surgery in 1 case only.[2] Complete removal of the intact hypophysis was attained by Dr. DONALD MATSON in the last half of 40 operations reported by JESSIMAN.[3] JESSIMAN, and PEARSON and RAY [2] have now suggested that results justify the use of this treatment in earlier cases. Further progress towards deciding whether durable remissions are obtainable seems to be barred by two main obstacles.

First, means have not yet been found for predicting which patients will react with the striking, though temporary, remissions which justify hypophysectomy. A second adverse factor may lie in the frequent—probably universal—persistence of the human pharyngeal hypophysis and the possibility that this undergoes compensatory functional hypertrophy after complete removal of the sellar pituitary. In all examples of pharyngeal hypophysis examined after hypophysectomy MÜLLER [4] found vascularised tissue containing typical eosinophil and chromophobe but no basophil cells. Whether these " activated " hypophyses function can be investigated only in man because pharyngeal hypophyses are not constantly present in laboratory animals. If, in fact, either prolactin or somatotrophin (growth hormone) or both are secreted by the " activated " eosinophil cells, preoperative hormonal conditions may be restored sufficiently to stimulate such tumour cells as remain dependent on hormones. A return of œstrogens in urine is common after bilateral ovariectomy, alone or combined with or succeeded by adrenalectomy.

The return of endogenous œstrogen and inability thereafter to eliminate this type of hormone appears to many to be a serious obstacle to obtaining remissions if these depend on complete elimination of all responsible hormones. The theoretical foundation for hypophysectomy is that continued growth of some neoplastic cells requires similar hormonal conditions to those needed for structural development of the normal breast. For the latter, œstrogen and pituitary hormones (prolactin or somatotrophin or both) are indispensable synergists. Without the steroid and the protein hormone or hormones acting in some way together, the

1. See *Lancet*, 1957, i, 515.
2. Pearson, O. H., Ray, B. S. *Cancer*, 1959, **12**, 85.
3. Jessiman, A. G. *Ann. R. Coll. Surg. Engl.* 1959, **24**, 213.
4. Müller, W. *in* Endocrine Aspects of Breast Cancer (edited by A. R. Currie); p. 106. London, 1958.

breast will not develop. Almost certainly both types are required also in initiation of breast tumours, and this is assumed to be the case with continued growth of "dependent" but not of autonomous neoplastic mammary cells. Evidence of the need for both types of hormone for growth of dependent cells is described by PEARSON and RAY.[2] Physiological doses of œstrogens were administered for thirty to sixty days to 5 patients with metastatic osseous breast cancer several weeks after hypophysectomy, to which they appeared to be responding favourably. In none was there any evidence of reactivation of tumour growth; and in all 5 objective improvement was subsequently seen. PEARSON and RAY conclude that their observations suggest that œstrogenic hormone does not stimulate growth of existing mammary cancer in the absence of the pituitary gland, and that some hormonal factor from or mediated by the pituitary is necessary for œstrogenic stimulation of tumour growth. It is not recorded, however, that these 5 patients survived any longer than the average, and subsequent activation of the pharyngeal hypophysis is not excluded. JESSIMAN[3] and his colleagues observed and measured a resurgence of œstrogenic activity accompanied by clinical progress of the disease in a patient about seven months after complete hypophysectomy, judged by satisfactory postoperative falls in follicle-stimulating hormone, radioactive-iodine uptake, and protein-bound iodine level. Necropsy showed absence of pituitary tissue in the sella turcica and confirmed the endocrinological studies. Nevertheless prolactin and somatotrophin may have recurred from a pharyngeal hypophysis, or after seven months the patient may have reached the end of her remission. The result of administering somatotrophin alone to 5 hypophysectomised patients[3] was not so clear-cut; and further observations are required, including concurrent tests for œstrogen. The results suggest, however, that growth hormone, alone or combined with added exogenous œstrogen, does not activate a tumour which is in remission. Prolactin was not tested. So far as the evidence goes, it seems that to determine whether dependence really exists it is probably unnecessary to eliminate completely more than one type of hormone—either a pituitary protein or an œstrogen. Of the two sources the pituitary is the more localised and accessible to complete ablation. If, in fact, the pharyngeal hypophysis is found to be a source of prolactin or somatotrophin it may prove to be destructible by some form of irradiation—for example, the technique described by LAWRENCE.[5] An anti-hormone[6] would reach products from both sources if administered continuously. The immunochemistry of anti-pituitary hormones has been explored by CURRIE et al.[7]

The merits of various ablative and hormonal antagonist treatments in relieving symptoms and in producing remissions will become clear when the results of these different procedures have been reported by a single group of workers. Permanent "dependence" has not yet been demonstrated. If it is to be sought by earlier ablative surgery, including presumably, mastectomy, records of survival-times for mastectomy alone or combined with irradiation, such as those published by HARNETT,[8] would provide useful material for comparison.

5. Lawrence, J. H. *Cancer*, 1957, **10**, 795.
6. *Lancet*, 1955, ii, 75.
7. Currie, A. R., Cruickshank, B., Hewitt, C. L., Dekanski, J. B. *in* Endocrine Aspects of Breast Cancer (edited by A. R. Currie); p. 122. London, 1958.

Annotations

INFLUENZA AND THE ENDOCRINE SYSTEM

AN inquiry into sudden death in infancy suggested that overlaying and accidental suffocation are probably less important contributory factors than respiratory infections, possibly due to viruses.[9] Reports from South Africa have clearly shown that Coxsackie-virus myocarditis, unless specifically sought, may be overlooked as a cause of sudden death.[10] Sudden deaths due to virus infections are not, of course, restricted to infancy; for in the 1957 Asian influenza pandemic, fulminant infection occasionally caused sudden death in previously healthy young adults.[11 12] In October, 1957, several sudden unexplained deaths in young persons came to the notice of the coroner's office in a Cleveland county. In the subsequent medicolegal investigation, necropsies disclosed hæmorrhagic œdematous bronchopneumonia often associated with an eosinophilic hyaline membrane outlining the alveolar spaces.[13] Accompanying virus studies showed that the sudden deaths were due to the Asian strain of the influenza virus. This Cleveland report also draws attention to the frequency of toxic or shock changes indicated by lipoid depletion of the adrenal glands, myocarditis in a third of the series, and cerebral swelling which in several cases produced a prominent cerebellar cone. Oseasohn et al.[13] stress that, although the major pathological interest in influenza has been rightly focused on the bulky, airless, hæmorrhagic and œdematous lungs, the frequency and intensity of these extrathoracic lesions indicate that influenza must be viewed as more than a purely respiratory infection.

In this issue, Dr. Mickerson takes this wider view in presenting his hypothesis that the pituitary-adrenal axis may be at fault, and spotlights once again the vexed and controversial problem of the value of corticosteroids in influenza. Jahn et al.[14] advocated corticosteroid therapy in overwhelming infections on the principle of "buying time", to halt deterioration long enough for antibiotics to take effect. Kinsell and Jahn[15] recommended the routine use of corticosteroids—with sulphonamides, for instance—in all patients with meningococcal septicæmia; but Lepper and Spies[16] were unable to establish any clear-cut gain from such a regime in septicæmic patients with or without meningococcal meningitis. In fulminant abacterial influenza the problem is different in that there is no effective antibiotic to administer as a safeguard with corticosteroid therapy. Any possible benefit from steroids would consist in countering transient adreno-

8. Harnett, W. L. *Brit. J. Cancer*, 1948, **2**, 212.
9. Banks, A. L. *Mon. Bull. Minist. Hlth Lab. Serv.* 1958, **17**, 182. See *Lancet*, 1958, ii, 513.
10. See *Lancet*, 1958 ii, 949.
11. Roberts, G. B. S. *ibid.* 1957, ii, 944.
12. Neilson, D. B. *Brit. med. J.* 1958, ii, 420.
13. Oseasohn, R., Adelson, L., Kaji, M. *New Engl. J. Med.* 1959, **260**, 509.
14. Jahn, J. P. et al. *J. Pediat.* 1954, **44**, 640.
15. Kinsell, L. W., Jahn, J. P. *Arch. intern. Med.* 1955, **96**, 418.
16. Lepper, M. H., Spies, H. W. *Antibiotics Ann.* 1956/57; p. 447.

cortical insufficiency and preventing flooding of the alveoli with serum.[17]

Further work will clarify the type and degree of any pituitary-adrenal dysfunction in the otherwise healthy influenza victim; but there can be little doubt that pre-existing adrenocortical insufficiency needs vigorous replacement therapy. In another article in this issue, Dr. Skanse and Dr. Miörner show that the mortality from Asian influenza in Malmö was highest among those with uncontrolled adrenocortical disease, whereas the illness ran a favourable course in similar patients who had received full substitution therapy. They make out a good case for not only checking the adequacy of corticosteroid substitution therapy in such patients when influenza is imminent, but also protecting these potentially susceptible people by influenza vaccination.

CORTICOSTEROIDS FOR TUBERCULOUS PLEURAL EFFUSION

IT was early observed that corticosteroid therapy may cause pulmonary tuberculosis to spread [18 19]; later it was discovered that, if effective chemotherapy was given concurrently, steroids did no harm and owing to their anti-inflammatory action might even do good.[20] This was confirmed by a controlled trial [21] which showed that prednisolone in these circumstances hastened clinical improvement and radiographic clearing, especially in patients with acute disease, although it had less effect on cavity closure and sputum conversion. The anti-inflammatory action of steroids would be expected to be particularly effective in tuberculous pleural effusion. Even et al.[22] reported good results in 54 cases, and Aspin and O'Hara [23] concluded, from a comparison of the findings in 16 steroid-treated patients with those in 14 patients treated only with standard drugs, that the addition of steroids to therapy greatly expedited absorption of fluid. Now Paley et al.[24] report favourable results in 26 cases of tuberculous pleural effusion treated with prednisone and antituberculous drugs.

As soon as the diagnosis was made, as much fluid as possible was removed and the patient was put on a regime of 300 mg. isoniazid daily, 1 g. streptomycin three times a week, and oral prednisone. Prednisone was given for four weeks: 30 mg. daily for four days, 20 mg. daily for seven to fourteen days according to the response, and 10 mg. daily thereafter. No intrapleural treatment was given. There was a striking clinical improvement in all cases, and, irrespective of the amount of fluid originally present, serial chest films showed rapid clearing of what remained after the original aspiration; in only 1 case did enough fluid re-accumulate to require a second thoracentesis. Whereas previous experience had been that fluid persisted for six months in 25% of cases, in the prednisone-treated cases it disappeared in three to six weeks with the result that the average stay in hospital was cut from six to two months. In 12 of the 26 cases absorption of fluid was so complete that no radiographic abnormality could be detected, and in the remainder the only evidence of previous disease was blunting of the costophrenic angle or slight basal pleural thickening. This suggests that steroid therapy may prevent that distressing sequel to pleural effusion—gross pleural thickening with serious impairment of lung function. 14 of the patients were followed for at least eighteen months, and recrudescence of disease was observed in none.

Evidence that steroids are valuable in the treatment of tuberculous pleural effusion continues, therefore, to accumulate: only the verdict of a controlled trial is needed to put the issue beyond doubt.

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18. Freeman, S., Fershing, J., Wang, C. C., Smith, L. C. *in* Proceedings of the First ACTH Conference; p. 509. Philadelphia, 1950.
19. Hart, P. D'A., Rees, R. J. W. *Lancet*, 1950, ii, 391.
20. Houghton, L. E. *ibid.* 1954, i, 595.
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22. Even, R., Delaude, A., Roujeau, R., Trocme, Y., Commare, G. *Rev. Tuberc., Paris*, 1955, **19**, 1249.
23. Aspin, J., O'Hara, H. *Brit. J. Tuberc.* 1958, **52**, 81.
24. Paley, S. S., Mihaly, J. P., Mais, E. L., Gittens, S. A., Lupini, B. *Amer. Rev. Tuberc.* 1959, **79**, 307.

NAMES FOR BLOOD-CLOTTING FACTORS

HÆMATOLOGY has been troubled with difficulties of nomenclature that have caused real confusion, and a lot of ink has been spilled in support of this or that system. The confusion over names for erythroblasts was settled years ago. The controversy over names for blood-groups was once serious when one system meant precisely the opposite of another; today only names for the Rh group are still argued about, and the patient is safe whichever of the two current systems a laboratory uses. The latest chapter of hæmatology to be involved in confusing multiplicity of names is that dealing with the blood-clotting factors: no less than 11 names have been proposed and used for so clearly defined a factor as the antihæmophilic globulin. This sort of thing is liable to result in misinterpretation by research-workers of each other's results, and patients with the less common abnormalities of blood-clotting may be treated in different ways according to the centre they attend. Warned by previous controversies and the many years it took to settle them, workers interested in research on blood-clotting got together as long as five years ago and set up a committee with Dr. Irving Wright of New York as chairman and Prof. R. B. Hunter of Dundee as vice-chairman. The committee has members in many countries, including most of the workers who were responsible for the confusion by naming clotting factors. The preliminary conclusions and first recommendations of this international committee have now been published in the *British Medical Journal* [1] and the *Journal of the American Medical Association.*

The committee had to choose between names that have been widely accepted for many years, symbols that carried no implication of function, and names that were accepted by many but did imply function. Wisely they did not consider an entirely new system; experience has shown that, however rational such systems may be, they are not likely to gain general acceptance. The committee decided that internationally acceptable names should not imply an action or a particular theory of blood-clotting, especially because factors that had been given a name which implied a particular function had later proved to have a different function. They therefore adopted a compromise:

(1) Some well-known and generally used names have been accepted because few alternatives have been proposed. These names are: fibrinogen, prothrombin, thromboplastin (tissue), and calcium. All these factors, except thromboplastin, can be defined and identified in chemical and physical terms. Fibrin might be added to this list; but presumably it has not been included because it is the end-product, not a clotting " factor ". Platelets also are not mentioned, presumably because everyone recognises them, though fractions with different actions have been prepared from them.

(2) For the other factors a numerical system is proposed; and, since roman numerals have already been used to designate

1. *Brit. med. J.* May 16, 1959, p. 1292.

some factors, it is proposed that these numbers should be adopted and the author could add, in brackets, any synonym he liked. For example, one could write factor V (pro-accelerin) or factor V (labile factor) according to whether Owren's or Quick's classification was being used. The roman numeral system has the advantage of being intelligible in any language, including oriental ones.

For acceptance and allotment of a number in this system, the committee proposes some minimum criteria:

(1) There should be valid and reproducible data on the effect of storage, adsorbability, inactivation by heat, and the effect of pH. Additional chemical data are considered highly desirable.

(2) A clinically identifiable state associated with an abnormality of the clotting mechanism is regarded as supporting evidence for the lack or excess of a factor.

(3) Methods of assay of physiological properties are to be listed.

By these criteria four factors in addition to the four named ones have been accepted by the committee and allotted roman numbers; they are: factor V *alias* pro-accelerin, labile factor, plasma prothrombin conversion factor, &c.; factor VII *alias* proconvertin, stable factor, serum prothrombin conversion accelerator, &c.; factor VIII *alias* antihæmophilic globulin, antihæmophilic globulin A, &c.; factor IX *alias* Christmas factor, antihæmophilic globulin B, plasma thromboplastic component, &c.

This is not, and is not intended to be, a comprehensive list. Factors VI and X seem to have fallen by the way. Plasma thromboplastin antecedent, the Hageman factor, the Stuart-Prower factor, and the Bridge anticoagulant are, it seems, as yet insufficiently characterised to be accepted for the international nomenclature. The platelet fractions, fortunately allotted arabic numbers by their describers, also fail to gain a recognised place.

This scheme has a lot to commend it. Future writers should put in the appropriate international number whatever local name they prefer, and we think that some of these names will persist—after all, antihæmophilic globulin is a lot more informative than factor VIII. Those who wish to describe new clotting factors will endeavour to ascertain the data which the committee propose as minimum criteria for acceptance. This list of minimum criteria may need amendment from time to time; but we suppose that the committee will review the situation now and again, and we note that it proposes later on to publish in detail the criteria on which it bases the recognition of factors V, VII, VIII, and IX.

DROWSING JERKS

NOCTURNAL myoclonic jerks are very common. Many people have them occasionally; but a few have them frequently and violently. Some neurologists—notably Symonds [1]—consider that the latter group may have a variant of epilepsy—a view supported by the occasional association with other and more obvious epileptic attacks in the same person, amelioration with anticonvulsant drugs, and the very occasional presence of electroencephalographic abnormalities. Oswald [2] has studied four cases in detail and argues that there is nothing to differentiate the occasional jerk on falling asleep from those that occur frequently in some people. He further suggests that their frequency may be related to mental tension, and that they are as likely to be psychogenic as epileptic. His electroencephalographic evidence was also against epilepsy, as the records showed a modified K-complex (an arousal pattern) at times of jerks rather than any specific spike discharge.

All would agree that the vast majority of these jerks are not epileptic in any clinical sense. In a very few cases, however, there is corollary evidence of epilepsy in the individual or family, and the jerks themselves are frequent and may be accompanied by other paroxysmal hypnogogic features. In these people they are probably epileptic but may simply reflect a greater tendency for synchronous neuronal discharge in these persons than in the normal at all levels of the nervous system, including the spinal cord and brainstem.

1. Symonds, C. P. *J. Neurol. Neurosurg. Psychiat.* 1953, **16**, 166.
2. Oswald, I. *Brain*, 1959, **82**, 92.

SHARKS

THE Englishman contemplating emigration to Australia is apt to be a little disconcerted by hair-raising stories about sharks on the Sydney beaches. The new book by Dr. Coppleson [1] should reassure him. For many years the author, a well-known Sydney surgeon, has collected facts on shark attacks from all available sources, and the result is a valuable reference book, not merely for timid immigrants but also for authorities responsible for public safety.

A shark attack is a horrible affair. The sudden scream, the struggling victim, and the bloodstained water combine to make a picture which Dr. Coppleson does not attempt to disguise. But there is another side to it, which he makes equally clear. First, attacks are very rare. For every Australian "taken" by a shark, three are struck by lightning. At Bondi, Sydney's largest and most popular ocean surfing beach, there has been no attack for over thirty years, and since the introduction of regular meshing (netting) there has been no trouble at any beach so protected. Even in Sydney Harbour, which is infested with scavenging sharks, the youngsters regularly capsize their small home-made yachts, which are mostly sail and keel, and yet are quite safe as long as they stay by the boat—to swim ashore being highly dangerous. There is also a tendency for groups of attacks to occur in circumstances which can be narrowly defined and often point strongly to the operation of a single "rogue" shark. When attacks do occur it is a remarkable fact that there is almost always someone (often a stranger, sometimes a child, not always even a swimmer) who does not hesitate to go straight out to drag the victim, or what is left of him, away from the shark—an impressive testimony to the courage of the ordinary man and woman in a really sudden and desperate emergency.

But while Dr. Coppleson's book, covering these and many other topics, is written for and will not disappoint the serious student, the tenseness is relieved in places by true stories about sharks which make fiction look silly and which even have a certain grim humour. These derive largely from the literally omnivorous habits of the shark. Recorded inventories of the contents of sharks' stomachs make dyspeptic reading—and may include anything from a kitchen washtub to a raincoat or a cow's skull. Whether this is due to pica, myopia, or simple greed, it is accompanied by an embarrassing but understandable habit of disgorging undigested *bonnes bouches* at unexpected moments. Mark Twain's story of the shark which laid the foundations of Cecil Rhodes' fortune by swimming to Australia in 10 days after swallowing a copy of *The Times*, and thus enabling him to corner the wool market, is

1. Shark Attack. By V. M. COPPLESON. London and Sydney: Angus & Robertson. 1959. Pp. 219. 25*s*.

apocryphal. But in 1799, when Britain and America were at war, the master of the American brig *Nancy* sought to avoid arrest off Haiti by H.M. cutter *Sparrow* by forging false ship's papers and throwing the real ones overboard. Seven weeks later the latter were recovered, string and all, from the maw of a shark caught by a naval officer near San Domingo, and were used to expose the fraudulent Yankee. Equally improbable but also true is the more recent case in which a shark caught near Sydney was put, alive, in the local aquarium, where it duly disgorged a human arm which was identified by tattoo marks and led to a series of murder trials which made legal history in New South Wales.

To anyone bent on crime at sea the moral is clear—if you throw anything overboard it is always liable to be brought up later and used in evidence against you.

PUBLIC HEALTH AND FAMILY DOCTOR

THE National Health Service provided for the first time a rational framework for the organisation of medical care, making possible the even distribution of medical services throughout the country and throughout all social classes. The National Health Service Act systematised the developments of a century in the three branches of the service. Certainly the Act shifted some demarcation lines—for example, the medical officer of health, who might have had a great accession of power, lost control of the erstwhile local-authority hospitals—but in essentials it accepted the traditional divisions. The conference on Public Health and the Family Doctor, held on May 23 and 24 by the College of General Practitioners and the Society of Medical Officers of Health, examined particularly that field of medical care where the local-authority doctor and the general practitioner have a common interest that overlaps the administrative boundary between them.

It is in personal health services that these doctors discover their common interest. Each has a historic sphere of influence in the care of the individual patient. When private practice was marked by competition for patients and fees, preventive medicine did not at first flourish—the practitioner concerned himself with illness. But towards the end of last century the growing political influence of the poorer classes, associated with the spread of education, led to a change in attitude to disease and health. In this situation important demonstrations of prevention of diseases, such as those by Ballantyne in antenatal care, Budin in infant welfare, and Philip in tuberculosis, stimulated the demand for personal preventive medicine. The obvious instrument to meet this need was the public-health service, which had by then a half-century's experience of preventing disease by control of the environment. Despite the rules regulating competition, which vested in the doctor an almost proprietary right in patients, local-authority practitioners began to participate in the personal care of patients. As veterans at the conference testified, there arose from this competition for patients a hostility which was accentuated by the disparate aims and forms of organisation of local health authorities and private practice.

By eliminating fees, the National Health Service removed much of the economic basis for this hostility; and at the same time the general practitioner was enabled to provide a wider range of service. In this setting, a new ideology of medical care has developed among forward-looking general practitioners.[1–5] The papers of Dr. John Fry, Dr. R. J. F. H. Pinsent, Prof. Fraser Brockington, and others at the conference outlined the principles. The general practitioner is seen as the leader of a domiciliary team providing comprehensive medical care. There is no divorce between promotive, preventive, and curative work. The family is regarded as the basic unit in practice. The intimate collaboration of medicosocial workers and home nurses based on practices is required to widen the scope of domiciliary care; health education, preventive health examinations, and screening techniques are incorporated into routine work. There is awareness also of the need to define the theoretical background of social medicine—epidemiology and the behavioural sciences such as sociology and social psychology—as a specialised body of knowledge which may be applied in any branch of practice but specially in general practice.

Family doctors and medical officers of health at the conference described how they had tried to practise this kind of medicine. Their accounts showed that there are still many difficulties. There is evidently much good will, and a desire to collaborate which stems from recognition of common aims in the care of the patient, the family, and the community. But conflict is inherent in the administrative structure. Arrangements under the N.H.S. tend to prevent a general practitioner from handling all aspects of personal medical care in the community. Hence we have the freely expressed resentment between him and the clinic doctor who deals with segments of personal care, defined by the age and the role of the patient—for example, as schoolchild or pregnant woman. On the other hand these arrangements bring under the local authority widely differing functions in personal and environmental medicine. These services have in common only the primary aim of prevention; and prevention is the duty of all who practise medicine.

Services might more rationally be divided according to function. The general practitioner could be regarded as the practitioner of personal medicine in all its aspects. By contrast, some see the essential function of the medical officer of health as the managing of persons and institutions. On this basis, it is suggested, he would be primarily an administrator, and would contribute to the organisation of medicine in the local authority, the hospital, and the general medical services.

Such a specialty of administrative medicine could, if desirable, be developed by creating a rewarding career structure, with mobility and flexibility between the various administrations. But a high quality of comprehensive medical care is, as speakers at the conference indicated, less easily attainable. In the words of Scott,[1] practitioners need time, tools, and training. Time could come from smaller lists and higher fees. The tools are not only facilities for investigation and preventive screening, but clerical help and aid from auxiliary workers. At present, training is given almost entirely in individual practices, by senior doctors to their juniors. But the future may see further development of general-practice teaching units, such as that at Edinburgh, which contain the essentials for a training in comprehensive medical care, and for the consolidation of a body of theoretical knowledge. Just as the teaching hospital sets standards for consultants, so the teaching general practice could set standards for future general practitioners.

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Special Articles

WHY DO THEY DO IT?

A Study of Pseudocide

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SOME people who apparently attempt suicide do not want to die. It is hard to find out why they act as they do; this paper describes some of the reasons. Very often the patient himself does not know what was in his mind, especially if he has taken drugs or alcohol which distort reasoning and cloud the memory. Despite the difficulties we found that after carefully, and sometimes repeatedly, questioning patients and their relatives, we were able to divide apparent suicidal actions into three classes:

1. *Serious* (they really intended to kill themselves).
2. *Doubtful* (they tried for death, but clung on to life).
3. *Spurious* (they never meant to kill themselves).

Our study was made on 34 consecutive patients whom we saw in the general wards of our hospital; we excluded patients with obvious mental illness admitted to the mental observation ward. All our patients had deliberately harmed themselves or taken an overdose of tablets.

Others have found several answers to the questions:

(a) Why do some people kill themselves? (Sainsbury 1955).

(b) Why do others attempt suicide but live? (Ettlinger and Flordh 1955, Stengel and Cook 1958).

(c) What happens to those who survive? (Batchelor and Napier 1954).

(d) Which patients are likely to try again? (Schmidt et al. 1954).

We cannot better this work. Our aim is to describe those patients who harm themselves, but do not aim to kill themselves. Out of 34 patients we exclude 12 serious suicide attempts and are left with 9 doubtful and 13 spurious cases.

DOUBTFUL SUICIDE ATTEMPTS

The origin of such attempts depends on the quality of the people afflicted, and the quantity of affliction they have to endure. Some people, because of their own frailty, find trivial obstacles hard to face, whereas others of tougher moral fibre understandably shrink from a situation which would make the strongest quail. Even a small difficulty may spark off an unexpected emotional explosion when it comes after a long period of misery. Here are some examples:

CASE 1.—A Hungarian girl, aged twenty, took 15 aspirins because she felt lonely when her Irish boy friend did not visit her at the weekend, and had been offhand when she telephoned him. She took the aspirins impulsively and was glad when she came to no harm. Next day a solicitous boy friend escorted a smiling girl from hospital.

Comment.—Suicide may have entered her mind, but the appeal value of her action was enormous.

CASE 2.—On the morning she was to appear in court on a charge of larceny a woman of fifty-two could not be roused. Her sister missed a box of 50 butobarbitone tablets. Vigorous treatment was needed and she was still drowsy 2 days later. After recovery we found that three motives had been uppermost in her mind when she took the tablets; the wish to die was not mentioned. She was ashamed of her impulsive shoplifting and wished to do penance; she wanted to escape the consequences; she wished to gain the sympathy of those around her, and she wished to show her remorse. She was treated leniently by the court who were probably not influenced by her suicide attempt. For several months there was a lull in the constant family wrangling amid which she lived. After a family quarrel 2 years later she took another large dose of butobarbitone, this time more dramatically. After recovery a psychiatrist saw her but did not think that she needed psychiatric treatment. Her own doctor, who knows her well, thinks that both suicide attempts have been gestures to scare her relatives.

Besides the motives she admitted, it is possible that this lady was gambling with death. Her action had the "ordeal character" so well described by Stengel and Cook (1958). This is a superstitious feeling: "I'll try and kill myself, and if I fail it means I am not meant to die." Once the attempt has been made and has failed, there is a sense of expiation. Such ordeals can be very dangerous because these people may wish to load the dice so that survival is likely, but in ignorance select a way of hurting themselves which is lethal.

CASE 3.—A schoolboy of fourteen took 10 carbromal tablets. He said he took them because he was teased and thought stupid by his friends. Next day he freely discussed his troubles and seemed to have a normal outlook again. The death of his mother a year before had probably upset him more than he would admit. He was anxious to return to school without further ado and we agreed to this, as we thought having to see a psychiatrist might make his sense of inferiority worse. We wrote to his father 3 years later and found that he has been very well since; he has many friends and is happily settled in a good job.

Comment.—A boy with low gumption who reacted excessively to normal childhood teasing, probably because he was very unhappy after the death of his mother.

SPURIOUS SUICIDE ATTEMPTS

People failing in a serious attempt at suicide often deny they had any intention of killing themselves, so one has to be very careful before putting anyone in this group. All the same we were quite satisfied that over a third of patients in this series never meant to kill themselves. There were 13 such people and we classify their motives roughly thus:

Hysterical gesture	3
Attempt to get sleep	5
Escape from reality	2
Tantrums	3

This may be oversimplification, but we believe that these were the main motives. Here are illustrative examples from each group:

CASE 4.—An Irish maid of twenty, working in a hotel, gave in her notice and was due to leave the next day. Having no friends in England and only a week's wages she felt that desperate action was needed. She swallowed a bottle of aspirins and then, having told the manageress what she had done, she undressed and went to bed. The doctor, urgently summoned, found her sitting up in bed combing her hair, but as he entered the room she fell back groaning.

2 years before in another job she used to climb on to the narrow sill outside the maid's dormitory. "It used to make

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them scream and think I was brave," she told us. The almoner found her a place at a hostel, but we soon heard that she was making similar demonstrations there.

Comment.—A silly girl who liked showing off.

CASE 5.—An aggressive unlikeable man aged forty-two took to drink, bringing noise and violence to his home. His wife began divorce proceedings on the grounds of cruelty and at the same time she stopped cooking for him. After taking 12 phenobarbitone and belladonna tablets the husband admitted that he aimed to deflect his wife from the divorce proceedings. He failed and 9 months later the wife obtained her divorce.

These were two completely insincere attempts, but others belong to the type " now they'll be sorry ", a childish feeling of " this is going to show them—now they'll know what I have been suffering ". Such attempts are a form of sensational self-advertising akin to the self-starvation of the suffragettes, but with selfish motives. It may occur in children at loggerheads with their parents, in parents who feel neglected by their children, in unhappy marriages, and in hot-blooded young men who, in Damon Runyan's inimitable phrase, have " the big burnt-up feeling that a guy gets when his doll walks out on him ". Depending on the capacity for self-deception, such attempts vary from deliberate fakes to semi-convincing efforts where the patient nearly believes he wants to kill himself while taking good care that he doesn't.

CASE 6.—A foreign girl was admitted from her lodgings comatose after an overdose of sleeping tablets. We found that, being tired at the end of a long day's work, and kept awake by noise in the house, she took an overdose of sleeping tablets to make sure she got off to sleep.

Insomnia can lead patients to take an imprudently large dose of drugs with little regard to the risk. Such actions are difficult to assess because the insomnia may be due to depression, and it is then hard to know whether the overdose was suicidal, or taken simply to escape from the unbearable wretchedness of melancholic insomnia. Further, hypnotic drugs may produce a drunken state instead of sleep, and then more drugs may be taken without any clear motive at all. Later there is no memory of the events, which remain a mystery or are labelled " attempted suicide ". This is the " serial consumption " described by Ettlinger and Flordh (1955).

CASE 7.—A married man of twenty-nine started an affair with a girl of eighteen. His wife got wind of it and started divorce proceedings. The girl's parents made vigorous protests and finally sent a solicitor's letter. The girl and he were playing leading roles in the local dramatic society, and her parents successfully (and justly) set the rest of the cast against him. A few days before the first performance, he felt he could stand it no longer and took 50 phenobarbitone tablets which he promptly vomited. Afterwards he denied any suicidal intention. " Everything seemed to well up inside me " and he took the tablets on impulse. His wife obtained a divorce on grounds of adultery 6 months later and he married the girl with whom he is now living happily.

Comment.—A man faced with an intolerable situation needed a short holiday in oblivion.

CASE 8.—A man damaged his car one morning and arrived home in a bad temper. His wife, who was cooking the dinner, accidentally got in his way as he went to get ice from the refrigerator. He abused her for obstructing him and she answered back. The atmosphere was electric for the rest of the day, and the wife took 10 phenobarbitone tablets to calm herself. She became frightened at what she had done and was admitted to hospital without even becoming drowsy. Next day she was heartily ashamed of the result of the family tiff.

CASE 9.—The family life of a couple and four children became strained when the father began to indulge in drinking bouts every few weeks. A year before we saw her, the mother had had to call in the police because of his violence, but no legal action was taken. The night she came to us, he arrived home drunk and beat her because no meal was ready for him. He left in a rage and she impulsively took 40 tablets, an action which she later bitterly regretted. They seemed more settled a few weeks later, so perhaps her action brought father to his senses, though we doubt if this is why she took the tablets.

Situations like this produce a sudden desire not for death but " to get away from it all " plus a desire to " do something drastic ". The emotion is similar to the fury and frustration of a child as he stamps on his favourite toy. Sometimes it takes the form of going " on the blind " with alcohol, but if drugs are taken as well as alcohol an unexpectedly potent combination results.

CAUTIONARY TALES

It is inevitable that misjudgments are made. One mistake is to assume that people who harm themselves with no suicidal intentions, are safe if they do it again. The wife who puts her head into the gas oven as she hears her husband's step in the hall may die if he goes out again to get an evening paper. Playing with suicide, however insincerely, is playing with death. This may account for the following sad tale.

CASE 10.—A woman of twenty-six had an unhappy marriage and married again 1 month before we saw her. She had not been sleeping well and was admitted comatose in the early hours of the morning, said to have taken 8 sleeping tablets after a quarrel. After recovery she was reticent about her personal affairs and, as no psychiatric abnormality was found, she was discharged. 6 weeks later after a quarrel with her husband she went into the bathroom, came back with a medicine bottle and drank the contents. She collapsed immediately and was dead when brought to hospital 50 min. later. Dr. Donald Teare found at necropsy that she had aspirated vomit after drinking chloral.

Anyone who has made themselves seriously ill once, is more likely to do so again. The depth of her coma on admission suggests that she had taken more than 8 tablets, and this, together with her insomnia and her reticent manner, should have had more notice paid to them. Even so, it is unlikely that she would have accepted and benefited from treatment.

An easy mistake is to underestimate depression which often lifts temporarily after a suicide attempt. Depressed patients are particularly good at rationalising a suicidal action, making it appear accidental. The following story deceived all who heard it.

CASE 11.—A woman was admitted with a doctor's letter which said that she was depressed and had tried to gas herself. She herself said that while cooking the dinner she squatted down to baste the joint, and as she stood up she felt rather giddy. She then bent down to light the gas under a saucepan by her favourite method of sucking the cigarette in her lips into a brighter glow. This is the last thing that she remembered. Her husband, when seen, said: " I have told her a thousand times that it is a silly trick. You will do it once too often, my girl, and blow your b—— head off."

The story was so convincing that she was discharged after a few days' observation during which she appeared tense but otherwise normal. Within a few weeks she was admitted to a mental hospital with anxiety, but without much depression.

She failed to return from home leave 18 months later and was still overanxious when she left hospital.

Comment.—We still do not know whether she attempted suicide or not. If she did, she told a perfect story.

DISCUSSION

You may think that we have sketched our patients too boldly or too simply; we are only too conscious that motives are often more complex and mental upsets more deepseated than we have depicted. Stengel and Cook (1958) found that most people who kill themselves take good care not to be thwarted, but those who harm themselves and recover are " Janus-faced, with one aspect directed towards destruction and death, and the other towards human contact and life ". Our patients did not even seek death halfheartedly; they did not aim to die at all. Motives in cases usually classified as attempted suicide range from singleminded, coldly planned self-destruction, through irresolute attempts in which the person is unnerved by a love of life, and reckless actions without thought for the consequences, to trivial gestures such as the dramatic taking of 5 aspirins by a thwarted lover. To divide people who have harmed themselves into those who deliberately risked death, and those who had no thought of death, is artificial but broadly true. There is an overlap with those who kill themselves, because some patients die who do not want to, and some patients live who genuinely desired to die.

In our experience, of those admitted to hospital alleged to have attempted suicide, one in three did not want to die. They were not cases of attempted suicide; we call their performance " pseudocide "—a monstrous word which we would gladly relinquish if we knew as good a current one. The motives for pseudocide may be difficult or impossible to determine. Often, however, the action was performed simply for its effect on others, to obtain sleep or temporary escape, or as a childish tantrum in which the motives were crude and fleeting.

Batchelor and Napier (1954) have shown that a bold policy of discharge from hospital is justified by results. When the suicidal motive is small or nonexistent it seems right with patients such as we have described to send them home soon and arrange outpatient psychiatric or social help if necessary. Misjudgments are inevitable; the most serious is to underestimate depression. Unstable people may kill themselves during another tantrum, but this cannot be prevented except by removing the cause of the quarrels. Usually the patients we have described have acted childishly and unthinkingly, and when they recover they are anxious to join the stream of life again with as little fuss as possible.

SUMMARY

People are described who deliberately harm themselves or take an overdose of tablets without wishing to die. We have termed these actions " pseudocide ".

Pseudocide may be a hysterical gesture, or its purpose may be to escape from reality, or to get sleep.

Misjudgments by the patient or doctor may have fatal results, especially as many doctors tend to underestimate the degree of the patient's depression.

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GENERAL MEDICAL COUNCIL

IN his address at the opening of the Council's 198th session on May 26, Sir DAVID CAMPBELL, the president, said that since 1858 it had been the right and indeed the duty of the Council to ask licensing bodies to provide information as to the courses of study and examinations required of candidates for their qualifications. For this purpose the Council, almost from the outset, asked bodies to send annually particulars of the results of the examinations which they had held in the preceding year. In 1877 a member of the Council, Dr. Aquilla Smith, produced an interesting analysis which showed that throughout the previous 15 years the number of rejections in final examinations had steadily increased, from 12% in 1861 to 23% in 1875. This was held to prove that examination requirements had " increased in much greater proportion than the attainments of the candidates ", whose rejections had been due in the main to " want of diligence ". The Council were called upon to make further efforts to raise the standard of the education of candidates more nearly to a level with the standard of the examinations. An important innovation was made at a much later date, in 1901, when the Council decided that licensing bodies should annually furnish the Council with a detailed list of the exemptions granted by them in the examinations which they held. There was then found to be a wide divergence among licensing bodies as to the exemptions granted by them to students who had passed elsewhere in some subjects.

The annual examination returns now before the Council revealed wide diversity of practice between the different licensing bodies both in the arrangement of examinations and in the conditions under which candidates were permitted to enter for them. This diversity pervaded the entire curriculum from the premedical to the final examination. On the whole it was to be welcomed. In the past the criticism has been made that the effect of the Council's Recommendations as to the Medical Curriculum had been to restrict the freedom of bodies and schools to make experiments. The Council, however, had neither attempted nor desired to promote uniformity, and the diversity of arrangements revealed in the returns stood in clear contrast to the situation in other countries where arrangements for medical education and examinations were directly controlled by a central authority.

In the past ten years there had been at least two attempts to impersonate practitioners whose names appeared in the Register. Such cases were normally a matter for the police, but in a third case the Disciplinary Committee were called on to erase from the Register an entry which had been fraudulently caused to be made by a person who had impersonated a qualified Canadian doctor. In that case the Council were not the only body to have been deceived, for the impostor had previously not only caused his assumed name to be entered in the Register of a Canadian province but had also served for a time, and apparently not without some success, as a surgeon in a ship of the Canadian Navy engaged in operations during the war in Korea. More recently two cases of a different kind had occurred. In these cases two practitioners from overseas, who were in all probability properly entitled to be registered, found it inconvenient to produce genuine evidence of the experience now required for full registration and produced instead some documents which were open to question. The persons concerned were subsequently prosecuted and pleaded guilty to offences under the Perjury Act, 1911.

Public Health

AN EPIDEMIC OF UNKNOWN ÆTIOLOGY

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MANY epidemics of unknown ætiology are seen each year in general practice.[1] Consultant colleagues see these cases only when complications develop, when the illness cannot be adequately treated at home, or when there is an outbreak among hospital staff.[2] Likewise public-health authorities seldom hear about these maladies, since they are not notifiable. In these short-term illnesses a diagnosis of "influenza" is frequently made, although influenza virus is rarely isolated.

The urban patients of this general practice are fairly evenly distributed throughout the city, and most of the rural ones live within six miles of the central surgery. The sex and age distribution is very close to that of the national average, and does not deviate by more than 0·6% from the average in any group.

TABLE I—THE AGE-GROUP AND SEX-DISTRIBUTION OF CASES

Age-group (years)	Sex		Number of cases
	M	F	
0–10	3	4	7
11–20	4	2	6
21–30	6	3	9
31–40	2	3	5
41–50	2	8	10
51–60	3	2	5
61–70	2	3	5
71+	0	1	1
Total	22	26	48

The small epidemic described here was first recognised on March 29, 1957. I diagnosed 5 cases in retrospect, 24 during the next two weeks, and the remaining 19 over the following five weeks. The sexes were equally affected in each age-group (table I). General practitioners were notified of the outbreak[3] and positive returns were received from Worcester, Malvern, Coventry, and Callington (Cornwall). The College of General Practitioners named this symptom-complex L.W.57.

TABLE II—FREQUENCY OF SYMPTOMS AT INITIAL EXAMINATION

Symptoms	Cases	Symptoms	Cases
Headache	48	Diarrhœa	7
Nausea	35	Abdominal pains	6
Giddiness	30	Insomnia	5
Sore eyes	19	Chest pains	4
Vomiting	16	Constipation	4
Sore throat	11	Photophobia	3
		Cough	1

Within three days of the onset of symptoms, whenever possible, freshly passed fæces were collected in a universal container, one throat swab was immersed in Hank's medium and a second in broth medium, and blood was taken with a dry syringe. All specimens were delivered to the laboratory without delay and the fæces and throat swabs were stored in a deep freeze. A second or convalescent specimen of blood was taken at about the third week of the illness.

1. Langdale-Smith, H. G., Langdale-Smith, D. M., Wilkinson, B. R. *Lancet*, 1957, i, 805.
2. Ramsay, A. M. *ibid.* 1957, ii, 1196.
3. College of General Practitioners. Research Newsletter no. 15, p. 188. 1957.

Clinical Findings

A conspicuous feature of all the 48 cases was the sudden onset of symptoms; 31 patients reported within forty-eight hours of their first symptoms. 35 had hitherto been in excellent health. There were several symptoms, all of which occurred suddenly (table II).

No evidence was available to give any indication of an incubation period, although 2 cases were from one family and 3 others from an institution. In both instances, all developed symptoms within twenty-four hours of the first case.

TABLE III—FREQUENCY OF PHYSICAL SIGNS AT INITIAL EXAMINATION

Physical sign	Cases	Physical sign	Cases
Bilateral conjunctivitis	14	Fauces injected	6
Fever of 99°F to 101°F	13	Furred tongue	3
Slight neck rigidity	8	Tremor	2

The principal symptom was severe headache in 43 cases, nausea in 2, giddiness in 2, and vomiting in 1.

All the patients had headache for a day or two. 43 of them had innumerable attacks of headache coming on every few minutes, while in the other 5 cases the headache was constant. In 45 the site was the frontal area, and in the remaining 3 it was temporal or occipital.

Nausea was a symptom in 35 patients and 15 of these vomited once or more. 30 patients complained of giddiness and 29 had sore eyes and/or sore throat. Bowel disturbances, abdominal pains, chest pains, insomnia, and photophobia were present in a few cases.

Positive physical signs were elicited in 24 cases (table III). No patient had enlarged cervical glands, postnasal mucopus, nasal signs, or changes in the voice. The frequency of the combination of signs and/or symptoms is shown in table IV. 18 patients had intermittent frontal headaches, nausea, giddiness, eye and/or throat (E/T) symptoms and/or signs. The remaining 30 had various groupings of these symptoms and/or signs.

TABLE IV—COMBINATIONS OF SIGNS AND/OR SYMPTOMS

Signs and symptoms				Cases
Headache	Nausea	E/T	Giddiness	18
Headache	Nausea			8
Headache			Giddiness	6
Headache		E/T	Giddiness	6
Headache	Nausea		Giddiness	5
Headache		E/T		4
Headache		E/T	Giddiness	1
Total 48	31	29	36	48

Investigations

Laboratory investigations and chest radiography were carried out in 30 cases (table V). The specimens were taken from 28 patients and delivered personally to the laboratory without delay. No virus was isolated from the sixteen specimens of fæces using HeLa-cell culture and monkey-kidney tissue-cell culture. Similarly no virus was isolated from sixteen throat-swabs using egg, HeLa cells

TABLE V—LABORATORY INVESTIGATIONS AND CHEST RADIOGRAPHY

Investigation	Cases	Medium	Result
Fæces	16	HeLa cell	All negative
		Monkey kidney	" "
Throat-swabs	8	HeLa cell	" "
		Monkey kidney	" "
		Egg	" "
Blood taken within 3 days of onset of illness	10	Serology	" "
Convalescent blood	19	Serology	" "
Chest X-ray	7	X ray	All normal

and monkey-kidney tissue cells. All the serological investigations on the ten initial and the nineteen convalescent bloods were negative. Seven chest radiographs and several other routine laboratory tests showed no abnormal findings.

Summary and Conclusions

In a small epidemic of a disease resembling influenza seen in a Worcester general practice a group of 48 patients with similar symptoms and signs was investigated. 18 patients who had previously enjoyed good health developed sudden intermittent frontal headaches associated with giddiness, nausea, vomiting, sore eyes, and sore throats. Most cases were apyrexial and a few had bilateral conjunctivitis, slight neck rigidity, and injected fauces. These signs and symptoms lasted one or two days and complete recovery occurred within seven days. Treatment was symptomatic.

The history and the course of the illnesses suggested infection by a virus, but no virus was isolated from the sixteen specimens of fæces or from the eight pairs of throat swabs. Nor did serological investigations on twenty-nine blood specimens demonstrate any rise in antibody titre which might have been evoked by such an illness.

My thanks are due to Dr. G. I. Watson, director of the College of General Practitioners' epidemic observation unit, for advice; to Dr. R. J. Henderson, bacteriologist to the Public Health Laboratory, Worcester; and to the Central Virus Laboratory at Colindale for the many laboratory investigations.

Infant Mortality and Stillbirths

The latest volume in the General Register Office series of Studies on Medical and Population Subjects includes basic statistical data derived from a large-scale inquiry into the social and biological factors affecting the deaths of children in infancy.[1] The inquiry, carried out jointly by the Social Medicine Research Unit of the Medical Research Council and by the General Register Office, was concerned with the deaths in infancy of children born in 1949 and 1950 in England and Wales.

1. Studies on Medical and Population Subjects no. 15: Social and Biological Factors in Infant Mortality. H.M. Stationery Office. 1959. Pp. 195. £1.

The Widdicombe File

LIV. WORK IN THE WORKS

DEAR GEORGE,

I'm very glad indeed to hear that you've decided to take the plunge and enter industrial medicine. But you'll find it different from anything you've done before. Not in its content, because patients are the same all the world over, but in its approach and its relationships.

People work, by and large, to earn money to buy themselves and their families as large a share of the world's goods as they can. Some really enjoy their jobs and get satisfaction from doing them—which isn't the same as saying that you or I would be satisfied with their jobs. (I once had a sanitary corporal in my regiment who took a real pride in his latrine buckets, all credit to him.) But many jobs are inevitably dull and frustrating and the opportunities for advancement negligible.

From the beginning, then, you'll not only be one of the team (spelt with a large or small " t " depending on your Managing Director), but also part of an intricate and constantly changing pattern of human relationships; and all your recommendations and suggestions will have to be seen against this background. Life can be very difficult for the production people at times. Ground between the upper and nether millstones of increased production on the one hand and improved conditions and shorter hours on the other, it is sometimes impossible to walk the tightrope of ideal Management.

I have a Manager just now who came up the hard way, industrious but rather humourless. He's cracking under the strain of a job that's just a little too big for him. Who does he talk to? If you're any good at your job he comes to you and asks your advice, especially about the physical symptoms which are the first cracks in the ceiling before the plaster comes down. This is one of the hardest and most rewarding jobs in industrial medicine. The confidences of the patient are inviolate, so that one can't intercede with the Directors on his behalf unless he agrees. Maybe he needs a temporary withdrawal from production on to planning or research staff to allow him to recover his equilibrium, just as the battle-weary officer would be withdrawn to a base job in war. One is asked for one's opinion: " What about old So-and-So, doc., he's not looking too good. Is the job getting him down? " Remember that you'll wield tremendous power (it would frighten you if you thought of it) to alter men's lives; your opinions will be listened to by all from the Chairman down, and a man's career may depend on your recommendations. So ponder your words and think, in the watches of the night if you wish, of the import of what you do. Always remembering that you're not an actor on the stage but rather the prompter.

Whatever industry you enter will have its own individual fascination. It's been my lot to work in heavy industries; so I'm almost certainly biased. I think that the heavier and more arduous the task the more character and spirit one meets among the workmen. If you expect the gentilities of a West End private practice you'll be disappointed. Instead you'll come to know men who are indistinguishable from the rock they hew or the steel they fashion but whose qualities will command at first your respect and later your wholehearted admiration.

You doubtless read the journals as I do and see how much in the last ten years they are taken up with questions of pay and conditions of service. If you remembered what I told you, you'll have examined most carefully your own contract and conditions of service and have driven as good a bargain with your employer as possible.

One day soon you'll see a man whose femur has been fractured while at work. Overnight his income drops from £15 a week perhaps to £6 7*s*. He doesn't grumble; he's very grateful to your medical service for what you do, and he speaks of the orthopædic registrar who looks after him in the ward with awed reverence. When he hobbles back to work, to a light job on light money, he's once again grateful to you because you help him on the road back. The money laboriously saved for a summer holiday may have gone to clothe the children and pay the rent. But he accepts it as part of the job. Could you face a cut of 50% on your salary with equanimity? I don't think I could.

Every industry has its lunatic fringe, its workshys, and its inadequate personalities and psychopaths. They're in the minority but they get more than their fair share of publicity. As I grow older (I had to give up playing rugger last year or face a divorce!) I see some of my younger colleagues confidently proclaim that A. B. is a malingerer. You know, when I can't find anything wrong the first

thing I suspect is that my examination has not been good enough. I wish I had a pound note for every paper written to tell me how to distinguish the true back injury from the leadswinger. Have you ever hurt your back? Better still, wait till the Chairman comes in with a pain he got on the 14th tee or in the rose garden. Listen to the song-and-dance he makes, and next time you hear about all those so-and-sos with bad backs at the Management Luncheon Club just smile and say nothing. In industry, as elsewhere, speech is silver but silence is golden.

Always keep a set of old clothes in your consulting-room or car so that you can go round your plant. I remember my disillusionment on meeting my Chief Medical Officer when I was a young and bright-eyed recruit to the firm. Thinking to show him the plant, I said, "What would you like to see, Sir?" "A large pink gin," was the prompt reply. The plant may look the same from week to week and may be singularly uninviting in rain, fog, slush, or (rarely) the heat of an August sun. But that is where your patients work, and that is where they will talk to you, and that is where you will really learn what they do. After ten years I learn something new each time and I enjoy listening to men tell me about their work and showing me their quiet, rather shy, pride in a job well done.

A last word about money. One of the most irritating platitudes which will grate on you is that "A good medical service pays for itself". Surely this misses the point. Medical services are provided because workpeople are human beings and not machines. Surely it should be the philosophy of a forward-looking nation to make work as attractive, safe, and healthy as possible. You should be there because your employer believes in you and your work, not because you save him money. And you don't, really, if you are honest. What you do is to increase the efficiency of the labour force, reduce the time lost from accidents and sickness, and make a lot of people a lot happier in their work because they know they can come and talk to you and blow off steam in privacy.

All this doesn't mean that you mustn't soil your hands with filthy lucre. On the contrary. If you're going to run a department you must be prepared to spend time in learning a little about costing and accountancy. You're no worse a doctor because you stoop to inquire the average cost per attendance in dressings or work out the cost of your service per employee per annum. Every other department has to do the same, so why should you be exempt? On the other hand don't let the accountants rule you. An old friend of mine, David Clark, put it very well when he described the auditors as white ants "nibbling away and eroding the fabric of human relations and good feeling". As he said, they want watching unceasingly.

Enough of these ramblings. I know you won't take them too seriously, but it's a pleasure to have a reason for getting them off one's chest.

Yours affectionately,
UNCLE E.

Symposium

PSYCHOSOMATIC ASPECTS OF PÆDIATRICS

THE study group of the Society for Psychosomatic Research met on May 8–10 at the Royal College of Physicians of London to discuss this subject. As one speaker put it, there were few facts to give but many questions to ask.

Constipation and Encopresis

Dr. MALCOLM MACGREGOR saw encopresis as the result of constipation and not as a separate condition. Over half his patients were youngest children, suggesting that lack of attention might play an important part.

Dr. JOHN KEMPTON discussed the erotic aspect of anal function, pointing out that the child's first "duty" was continence of fæces. Family attitudes varied from affection and tranquillity to forceful adaptation to the social mould. Among 67 cases of encopresis there were 4 boys to each girl and a history of several years before referral. Most children had massive rectal impaction with overflow incontinence when first seen: 10% had some degree of mental defect and no less than 85% came from "unsatisfactory" or unstable homes.

Dr. DOUGLAS GAIRDNER thought some cases were congenital rather than acquired, although histories from the mother became increasingly misleading as time passed, so that a child whose disorder dated from the age of two months might later be described as "difficult from the first". It was often hard to decide which of a group of associated disorders came first. He advised treatment with an initial enema (though in many cases the bowel was empty) and laxatives, perhaps over a long period.

Dr. P. BRAESTRUP described experiences in Copenhagen with 73 children with encopresis, of whom all but 3 recovered with simple enemas and routine care. Enuresis, when it accompanied encopresis, did less well, only half the cases remitting. Poor general condition and the presence of other physical complications were noted, but little in the way of underlying emotional disorder.

Dr. G. F. VAUGHAN said that of 1000 referred children of normal intelligence 10% were encopretic and 8% constipated. Half the cases, he thought, rose out of conflict, with too high a standard in the home, a quarter from the parents' low demands and I.Q., and the remainder from a non-specific response to stress. Encopresis was closely related to the mother's attitude, which was often sadomasochistic; he had known, for example, a mother become depressed and need treatment when soiling ceased. Dr. Vaughan saw an important connection between "dirty" toilet habits and "dirty" social ones such as lying and stealing.

Dr. MILDRED CREAK thought the meeting was skating round the problem of why some children chose this route although all were subject to tension and shocks? She believed that unconscious fantasy focusing on the bowel could produce structural changes.

Identification

Dr. JOSEPH SANDLER pointed to the similarity between parents and adopted, as well as natural, children. Primary identification led to the unconscious reflex of "echoing or reflecting", which occurred all the time in everyone from earliest infancy. Identification might be latent until circumstances evoke it—for example, mother's attitude to her child which would be determined by her mother's treatment of her. This mechanism could also account for contagion in the epidemiology of mental disorder, and physicians should be aware of it, inquiring into the patient's associations with others. The doctor should realise, too, that through identification with his patients he might tend to accumulate cases that had a particular meaning for him emotionally.

Recurrent Pains in Childhood

Dr. JOHN APLEY thought "suffering" might be a better term than "pains", since the parents rather than the child were so often involved. Normal children were essential as controls, but were rarely seen by pædiatricians. His survey in Bristol used the criteria of 3 months' history with at least 3 attacks; and among 700 children 4% had limb pain and 11% abdominal pain. The condition, therefore, was very common, and not all had been referred to hospital. Detailed investigation had revealed only 3% and 7% of organic illness in the limb and

abdominal groups respectively, and Dr. Apley now limited such tests to an E.S.R. for the former and routine urine for the latter, with occasional straight X-rays. He thought it very easy to over-investigate, particularly since 19 out of 20 pains were evidently of emotional origin. Follow-up, 8–20 years later, had shown that of 30 such cases virtually untreated, a third were quite well, a third still had bouts of abdominal pain, and the rest had other recurrent psychosomatic symptoms, notably migrainous headaches. Matched controls from the same clinic, seen for non-psychosomatic disorders, had very few of such features. A blind trial with phenobarbitone showed little effect but a tendency for the trouble to move to another part of the body. Comparing family histories with those of the controls, five times as many headaches and three times as many peptic ulcers were found. One speaker wondered whether pale stools with acetone in urine and breath indicated liver involvement in the abdominal syndrome, but Dr. Apley had found no disorder of liver function on testing.

Discussing concomitant psychiatric findings in this survey Dr. R. F. BARBOUR mentioned the difficulties of satisfactory work in a pædiatric outpatient department with other people in the room, a queue outside the door, and the history taken, perhaps, by someone else. Most of his group were between 8 and 11 years old and 50–60% of pains were related in some way to school stress: the increasing zeal of school-attendance officers was reflected in the clinics, for they left the child with illness as the only escape from a difficult situation. Such children were usually the youngest in the family, they were sensitive, nervous and inhibited, mixed poorly with others, and suffered from other disturbances such as poor sleep and nail-biting. About half had eating difficulties but incontinence was not usually a problem. Mothers tended to be older (a third were in the forties), half were nervous or in poor health, and often grandmother was still an important figure, though father was commonly passive. In time the pains came on with less and less stress and the disturbance often reflected mother's fear of parting from the child. Some parents were unamenable to psychiatric help because of mental defect or emotional difficulties, including inability to tolerate aggression, and to them, symptom-centred advice was offered; but helping one child often brought out difficulties in another. Dr. Barbour noticed that passing a treatable mother to the psychiatric social worker often made her feel "palmed off", reflecting lay scepticism about lay assistance. He wondered whether the classical hysterics now so rarely seen, were reappearing with psychosomatic illnesses.

Dr. CREAK emphasised the importance of seeing the child alone; the purpose of the pain should be sought, and she had known, for example, "pains in the chest" relate to the breasts and represent sexual anxieties. It was easy to over-emphasise a passing phase of anxiety: a warm bed and quiet comfort could settle the matter, whereas if G.P. and psychiatrist were called in there was no knowing where it might end.

Pædiatricians' Questions Answered

In a long session of skilful answers to questions, Miss ANNA FREUD said she believed that infants had a right to their own disturbances and that there was not always something wrong with mother: one child would cry itself to sleep and another into a panic. Sleep became related to personality development as the child related itself to the environment—for example, a dark still room or special toy. Why did pædiatricians seem so little interested in the effects of Soma upon Psyche? What did it mean to a child to go through some long and painful illness?

Psychological Development

Discussing the virtues and drawbacks of theories of psychological development, Dr. JOHN BOWLBY referred to the work of Piaget on the child's capacity to think about objects in time and space. The younger child seemed tethered to the "here and now" and his inability to imagine events occurring somewhere else tomorrow made it hard to prepare a 3-year-old for example, for going into hospital, and for a 2-year-old it was impossible. He thought, however, that Piaget was not interested in the development of personality, and neither were the learning theorists, towards whose views, as a psychoanalyst, he admitted a certain prejudice. Regarding the psychoanalytical school, he was somewhat heterodox in stressing so heavily the importance of experiment. He suggested that the "libidinal phases" of Freud were not supported by the evidence: it was a tidy theory explaining extragenital sexuality but it was probably wrong. Klein's views on the importance of the breast in the first 6 months, Dr. Bowlby thought, were of less import than the mother/child relationship over the first 2 or 3 years, and his film of rhesus monkeys showed a clear attachment to the mother-object that existed independently of food and that could be transferred to a wire dummy. Rhesus babies brought up without mothers showed much autoerotic behaviour. Future progress lay in the study of infants in their natural habitat—the home, as the ethologists had done with animals: a new class of data was required and he described interesting work at the Tavistock Clinic showing that activity in the child at home, notably crying, self-comforting, and social play, differed greatly according to whether the mother was normal, neglectful, or neurotic.

Theories of Psychosomatic Disorder

Dr. J. O. WISDOM said that psychological defences grew with visual imagery and that the capacity to deny, displace, repress, &c., was denied to the newborn who had no alternative to expressing tension kinæsthetically. He wondered whether the anxious child engendered guilt in the mother through which the child became able to manipulate the household. With infant feeding problems it was important to judge the case on its merits, looking both at the food and at the feeding process.

Diagnosis and Treatment

Psychiatrists, according to Dr. RONALD MAC KEITH, were able to cope without a fixed ætiological diagnosis for their patients, but pædiatricians were usually not. In the field of psychosomatic disorders a diagnostic label was clearly helpful but the ætiology was multifactorial—a fact increasingly recognised even in such organic conditions as infectious diseases. The constitution of the child was very important and in treatment it was better to assess him as a whole, as the psychiatrist did, rather than worry too much about an organ and why it was affected. The child should be allowed to talk and the symptoms viewed in their background, rather than rushing in with diagnosis and therapy.

Problems in Research

Dr. T. E. OPPÉ thought new methods of measuring affective elements were essential, but he wondered how far controls and statistics were useful. Dr. D. D. REID, from the epidemiological viewpoint, believed the most profitable investigation would be the prospective study, defining in detail the status of a group of cases and following them to see what happened. Such systematic observations, arduous though they were, should precede the formulation of hypotheses. Presenting an orthodox statistical view, Dr. DOUGLAS IRVINE explained that a hypothesis must be testable, otherwise it was useless.

Dr. EMMANUEL MILLER's closing address drew many topics together. Penfield and others had shown that the lowest somatic functions had cortical representation and that they were intimately related to the highest mental faculties: the infant's behaviour represented a "visceromotor combination". (Dr. CYRILLE KOUPERNIK also saw neurophysiological research as vital, and he pointed to the brain activating system as a basis for understanding affective responses). Fleeting autonomic changes, Dr. Miller thought, must be recorded at the youngest ages for there was then the closest relation between environment and effects on the body. It was better to speak of "autonomic patterns" rather than of emotions; subsequent patterns depended upon (and later regressed to) this "central autonomic disposition" and where it was inharmonious with inborn endowments or with the outside world the tissues were more vulnerable. The study of postures

in the pre-verbal and later stages was particularly important: personality differences between athletes had been correlated with style and movement.

The conference marked a further stage in collaboration between the organic and psychiatric approaches to child health and disease, and it showed how much the two branches need to help each other: the organisers are to be congratulated. The proceedings of the conference will be published in full elsewhere.

Medicine and the Law

A Delayed Ambulance

HAVING taken out for cleaning a tracheotomy tube inserted in his wife's throat after an operation for cancer, her husband was unable to get it back again. Neither could a doctor who was called to the house. The doctor telephoned for an ambulance, but it was two hours before it arrived and the woman died from asphyxia. These facts were related to the Manchester city coroner at an inquest on May 19.

In evidence, the doctor said there had been a previous occasion when the tube could not be put back in the woman's throat. The ambulance then arrived within 15 minutes. It was between 11.25 and 11.30 A.M. when he telephoned for the ambulance and a woman's voice replied that one would be around as soon as possible. He had asked for an ambulance to be sent to the woman's home right away. He mentioned on the telephone that it was a tracheotomy case and the patient would require a sitting ambulance. While he did not regard the situation then as an emergency he expected the ambulance to arrive within 15 minutes. He was again called to the woman's home at 1.35 P.M., just after the ambulance had been and gone, and found the patient had died.

A woman clerk at the ambulance depot said the doctor's telephone call was received by her at 11.55 A.M. and she recorded it at once in her book. She also wrote the letters SAP which meant " Soon as possible ". Answering the Coroner, she denied that she put in the time after she knew there was to be an inquest. She also denied that the doctor had mentioned the word tracheotomy or that he had said he wanted an ambulance right away. Because it was for a sitting case, she did not regard it as very urgent. It was untrue to suggest that she could have changed the time of the call later. An ambulance driver said when he arrived at the house, some time after 1 P.M., he found the woman was dead and he had the doctor called.

A legal representative of the husband pointed out that the duplicate records book of the ambulance depot showed five consecutive entries on May 8, the date of the woman's death, all marked with precisely the same time. Three other entries were similarly marked. He said that there was a possibility of the book being needed again, and asked that it should remain in the custody of the court.

The coroner recorded a verdict of misadventure and said he was inclined to accept the evidence of the doctor rather than that of the clerk. She should have realised the need was reasonably urgent. He thought the woman would be alive now if the ambulance had gone to her home at once. The dominant factor in the minds of some persons at the ambulance depot seemed to have been that it was a sitting case and, therefore, could wait. The doctor was in no way to be criticised for his behaviour for there could be no doubt that he had given the impression that the ambulance should be sent right away.

The coroner announced that he would impound the book.

Successful Application to Tribunal

The National Health Service Tribunal has granted an application by Dr. Alan Gray, of Woking, Surrey, that his disqualification for inclusion on any medical list should be ended. This disqualification was imposed in September, 1955.

In England Now

A Running Commentary by Peripatetic Correspondents

To the ageing practitioner, confused and bemused by new-fangled apparatus, new-fangled techniques, and the ocean of new specific drugs of weird nomenclature which make up correct practice these days, it is always cheering to see the bright boys brought up with a round turn. So you can imagine how pleased I was to see that the " astonishing results " in the treatment of cerebral abscess which my old teacher, Sir William Macewen, reported in 1893 " have yet to be repeated " [1] " Rag and bottle " chloroform anæsthetic, no X ray, no antibiotics, no electroencephalography, no ventriculography, none of the things we take for granted and yet these results. Astonishing—but is it when you remember that they were not attained by sleight of hand, but by accurate observation, sound anatomical knowledge, the application of basic physiology and pathology in exact nursing technique, and the aseptic methods which Macewen applied so rigidily in all his surgical work.

How far have we departed from this? For diagnosis, what touching faith in the laboratory and in the gadget, especially if it be mysterious, complicated, and electrical. The art and skill of observation and deduction—the educated eye, ear, and nose, the exploratory fingertips with their stores of impressions of hot and cold, of moist and dry, of muscle and skin-tone—are these things taught now, or practised in our hospitals?

The revenant spectre of hospital infections, raised by our misuse of potent drugs and our reliance on antibiotic umbrellas, now developing holes, haunts us again, because we have neglected the strict aseptic techniques which exorcised it so many years ago. But its return may be a blessing in disguise. If hospitals are to become again places of danger, as they were in pre-Lister days, we shall be deprived of our reliance on the gadgets which only they can provide, and be forced back on our knowledge of the art rather than the mechanics of medicine which can always be practised at the patient's bedside in his own home, whatever is done in hospital.

* * *

Charity begins at home; but to live in a block of flats, as I do, is to be a sitting target for door-to-door flag-sellers and collectors, each seeking financial support for some more or less worthy cause. The more remote the claim, the more difficult it is to dismiss. With the front door ajar, blank refusal seems impolite as well as uncharitable and discussion inevitably ends in capitulation. I have at last, however, found the perfect answer to this form of intrusion. In a drawer in the hall I have installed my *own* collecting-box—for " those poor, plastic children that are all the rage now ", as our Mrs. Mop sympathetically describes them. When the begging callers come to the door now, I immediately greet them with enthusiastic fellow-feeling. Their initial reaction of surprised alarm usually gives place to blank dismay when I proudly show and shake my own money-box. Subsequent financial arrangements are made only on a strictly reciprocal basis and the results are most encouraging.

* * *

Until last wet weekend I had been getting happily on with my work and ingesting my quota of the radioactive dusts raised by the blundering feet of Progress without noticing much mutating in myself or fellow-citizens. However, I now peer more closely at them through the haze of Strontium-90, because a novel of 1908 I read in a lonely farmhouse has made me realise the profundity of the anatomical and physiological changes in the Mother Race in the past 51 years.

For example, all males (1908 model) were between 6 ft. 2 in. and 6 ft. 4 in.; all were sun-bronzed, clean-limbed, clean-cut, and clear-eyed specimens of English manhood, except for a puny " Colonial " who was a mere 6 feet. Also, whereas everyone else had " the slender bones of the Aristocrat ", he had been issued with " hands like hams ". Even the villain was as

1. *J. Amer. med. Ass.* 1958, **168**, 868.

aristocratically ossified as the rest, but rather more bronzed as he was an " Arab sheik ". He was after the heroine's money, stupid fellow, instead of simply drilling an oil-well, and the action commenced at an English country-house party, where the lady distressed her hostess by refusing the services of a lady's maid and by using her legs instead of her thirty-horse-power limousine. Also she kept dropping things, whereupon the entire field of males would vault over the nearest hedge and pick them up. The uncouth Colonial was so overawed by these gentlemanly cavortings that " he flushed to the tips of his crisp brown hair ". This chameleon-like feat of physiology alone should have earned his admission to the Great House, but alas!, possibly because of disproportion between his hands and the finger-bowls, he was lodged in a " simple cottage " with one of the keepers. He was a quick learner, however, and could soon " put on a pipe " and cry, " No, no! It cannot be! " with the genuine 24-carat jeunesse dorée. His height also increased to 6 ft. 2 in., suggesting that male epiphyses fused later in 1908.

The expectation of life of these exemplary characters was lamentably low, the usual causes of death being drowning, shooting, brain fever, and mastication by wild animals. The poor Colonial, unfashionable to the last, fell off a cliff in chapter 7 while gathering the heroine's favourite flowers.

The remaining pages of the novel were missing, and the lady seemed booked to be an Old Maid. But when next my 5 feet 2 inches of pallid, bog-eyed British (English) manhood surveyed the bottle-shoulders and varicose-vein-festooned limbs in outpatients, I began to wonder whether all was indeed well with the Nation's chromosomery.

* * *

" Has the Blood Transfusion Service got a blazer-badge, Miss? " a donor asked our secretary last week.

" I don't think so," she said, " at least I've never heard of one. Why do you want one? Isn't your cricket club badge or your school badge good enough? "

" Well, it's like this," replied the donor, " I've got a smashing blazer, brand new, but I haven't got a badge. My school never had one, I was rejected for the Forces, I don't play cricket, and I don't swim or run. I just go for walks, and I do want a badge." This was too much for our kind secretary. " So you'd like two bleeding hearts! I'll write to the centre, and if necessary, I'll make you one myself."

Now then, Dr. Maycock, or whoever decides on these things, there's an idea. What about adding a blazer badge to the bronze, silver, and gold awards offered to regular donors. It might help us to enrol the younger generation to replace the old faithful donors as they retire.

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In the Garden.—IX

JARGON IS MY DARLING, THE YOUNG CULTIVAR

When I was young there were just species and varieties.
Species were mostly botanical and vars. were full of dubieties;
Species had Latin names and varieties were called Mum's Favourite;
Or if they came from France they were Souvenir de la Duchesse de la Rochefoucauld du Chateau Marguerite—
Which is why the English and French are different, and showed (what we always suspected) that gardening across the Channel was just a farce.
But now they're all called Jane Smith or Marie Dupont, on which the appropriate comment is Lord Curzon's when he heard that his Permanent Under Secretary of State had gone to luncheon before half-past one—" How very middle-clarse! "
Now we've got cultivars instead of vars, as we're so cultivated (" My dear, my chromosomes have come out in a rash! ")
And mutants and sports because we're so sporting (" Mine's a diploid and splash! ")
And gardening articles are so full of crosses they look like letters from a favourite niece.
Leave me in peace!

Letters to the Editor

MURDER AT THE CROSS-ROADS

SIR,—I think Dr. Geiringer (May 16) is pulling our legs a little with his gloomy prophecies of the doom of general practice. His fascinating picture of the " utility practitioner " reminds me of the recent brewery advertisement showing composite people whose appearance you can alter by placing different top or bottom halves over. Most of us have been utility doctors on occasions, both before and after 1948.

Dr. Geiringer's premise is that general practice in this country gives rock-bottom medical care. He thinks that this is due to the hospitalisation of medicine, and this in turn is conditioned by the economic structure of the N.H.S. with its capitation fee for G.P.s. His thesis is that the remedy lies in fee-for-service payment.

His premise is not true. The complaint that we are becoming mere signposts to hospitals or clerks to the N.H.I. fund has been voiced before, mainly by people who are not in general practice, as I have pointed out on a previous occasion.[1] The complaint is quite unjustified. There is indeed, as you say in your leading article of May 16, a very real renaissance of general practice, and had Dr. Geiringer gone around the country to visit medical practice, he would have found many family doctors practising at a very high level of medical care.

The facts as I know them are all against his claim that medicine is becoming progressively hospitalised or practised in clinics, owing to default by G.P.s. In our community of 50,000 people there are at least three practices which hold their own baby clinics. Most of the doctors I know do their own antenatal work. A good deal of psychotherapy is carried out by an ever-increasing number of family doctors. A good many doctors of my acquaintance carry out minor surgery and all sorts of specialised procedures in their own practices. There is far more real medical work done in general practices now than 10 years ago. But that does not necessarily mean that everybody must do everything. There is room in general practice for all sorts of people and manners of inclinations. Some family doctors develop special skills at the expense of other skills. Surely, not all shoes are made over one last. We are not Jacks-of-all-trades, so at times and on occasions we hand over certain activities to our consultants and hospitals. As an example, Dr. Geiringer complains that owing to the lack of economic incentive for G.P.s to buy electrocardiographs, coronary disease has become a " hospital disease ". I do not think that either the statement or the reason given is true. In illustration: I have no electrocardiograph, but our helpful local consultant physician will always come to domiciliary consultations with his apparatus, and he can take and interpret E.C.G.s much better than I. The patient still remains at home under my care.

Dr. Geiringer paints his wistful picture of the family doctor " in other countries—practising modern medicine in modern surgeries with clerical and laboratory help, choosing consultants personally, and retaining full charge of patients even when they have to go to hospital ". I could show Dr. Geiringer quite a number of practices in Britain where that holds good. In my district we have a cottage hospital where we G.P.s have full charge of our own patients. Many of us have modern surgeries with clerical help where we try to practise what I hope is modern medicine; we have free access to an excellent laboratory service; I for one choose my consultants personally, and my patients are usually seen by the chosen consultant.

No doubt there are black and grey spots in general practice, but improvements are always possible. It is part of the renaissance of general practice that the facilities mentioned and the desire to use them are becoming more widespread. I agree with Dr. Geiringer that the system of capitation payment gives no economic incentive for that, but I cannot really see that his

1. *Lancet*, 1951, ii, 1088.

fee-for-service payment with a fixed pool would do much better. The prospect of a scramble for the maximum number of services rendered is somewhat frightening. We are at present not reasonably well paid, but if we were, the exact method of payment would not be highly important, as you, Sir, rightly say, and, in any case, it would not make the difference between doom and rejuvenation of general practice. If we were reasonably well paid, an improvement of the level of general practice and an increase of the professional happiness and satisfaction of the family doctor could be achieved by professional, educational, and academic means.

The "utility practitioner" whom Dr. Geiringer describes so vividly as the end-product of the N.H.S. is not so much disappointed and frustrated because he does not use the technical skills he learned at medical school, but (to use Dr. Geiringer's words) because "his relationship with his patients is superficial and discontinuous and therefore poor in human satisfaction", and because his "numerous psychoneurotics are a great worry to the utility practitioner". In other words, he is a doctor who does not possess the skill of the family doctor to understand and use human relationships on the medical level. This skill is not taught at medical school. We general practitioners are becoming more and more aware that this is our specific skill, and that with its improvement the levels of general practice and of our professional satisfaction rise. And, as your correspondents have lately pointed out, the British Postgraduate Medical Federation refuses recognition as proper postgraduate courses to those courses for family doctors held at the Tavistock Clinic in London, teaching that skill and attended by G.P.s from all over the country.

And this is where we are truly at the cross-roads. Neither fee-for-service nor electrocardiographs for all will raise the level of general medical care, but the recognition by the profession as a whole that general practice is not just the left-over of the specialties, and that its specific skill should be taught at undergraduate and postgraduate levels, and studied as a proper scientific discipline.

When that day comes we shall have a real National *Health* Service.

Southall, Middlesex. MAX B. CLYNE.

SIR,—Dr. Geiringer's paper is useful in that it continues to focus attention on general practice. But it is rather overfilled with impressions, premises, and statements that certainly do not reflect the true state of general practice in Great Britain today. Since all these statements and impressions are not supported by facts it is essential to know the basis of Dr. Geiringer's information and also to know a little of his background: has he in fact had any wide experience of general practice in this country? How representative can his statements really be? As a family doctor with a fair experience of general practice in various parts of this country I should like to contest almost all his views.

The Bad Practice.—The implications seem to be that most of our practices come into this category. Has he in fact visited any appreciable number of practices in order to classify them as "good" or "bad"? What criteria apart from the very vague and general ones quoted did he employ? It is notoriously difficult to make a fair and accurate assessment of quality of medical care, as Collings, Osler Peterson, Hadfield, and others have found: did he employ any new and more satisfactory methods? Incidentally, in a most fair and widespread survey Hadfield [1] found that over 80%, of 200 practices visited and selected at random, could be classified as good or adequate. How bad are the "bad" practices? It is extraordinary that many of these are very large: can we ignore completely public discrimination and assessment?

1. *Brit. med. J.* 1953, ii, 683.

The Utility Practitioner.—It is hard to know to how many family doctors Dr. Geiringer's strictures are meant to apply. In very few practices can "relations be superficial and discontinuous", in almost none does the family doctor ever "play second fiddle to his consultant colleagues", and very many family doctors, including myself, hope that our sons will become G.P.s in Britain rather than anywhere else. Relationships with his patients and his colleagues depend on the individual doctor and have very little connections with the type of medical service in existence. Of course "numerous psychoneurotics" are a worry to all doctors all over the world, but let me assure Dr. Geiringer that they are not neglected as he supposes. We family doctors evolve our techniques of listening and endeavouring to help our patients with their problems. We do not "consider ourselves lucky" when these unfortunate patients decide to change their doctors. On the contrary, whenever a patient does change we hold a private and personal inquest to try and find out where we have failed that patient. We are by no means as mercenary as he believes, we still feel it our duty to cure the sick and we derive the greatest of pleasure in watching and assisting recovery. Pregnant women do not "go to the clinics with our blessings". We have considerable grudges against the clinic, school, and works doctors interfering with our patients. A very good proportion of family doctors run their own clinics for expectant mothers and children and are quite willing to take over the total care of schoolchildren. A similar proportion almost never refer cases for minor surgery to hospital departments. Does he realise the very small proportion of family doctors who have *ever* used the "emergency service", almost certainly less than 10%?

Hospitalisation of Medicine.—There are no figures at all to support Dr. Geiringer's suggestions that the G.P. is sending most of his seriously ill patients to hospital, but I can quote some personal figures against him. I carry out antenatal care for at least two-thirds of the pregnant women in my practice. I run afternoon clinics every afternoon, where I see the infants and children in my practice. Out of 500 acute chest infections (pneumonia and bronchitis) in the past five years only 3% required referral to hospital. Only 3 out of the 350 hypertensives in my practice have needed hospital treatment; only 7 of the last 50 coronary occlusions; only 3 of the last 25 patients with rheumatoid arthritis. Over a period of twelve months, out of 997 patients with skin disorders only 4% were referred to a consultant, only 5% of 663 "psychoneurotics", only 4% of E.N.T. cases, and 5% of eye cases. Is this really a picture of "hospitalisation of medicine"?

When he seeks to advocate the American system of each G.P. having and using his own E.C.G., X-ray, and pathology facilities, is he really on the right lines? Can one G.P. be the master of all three techniques? Is he aware that in over two-thirds of our hospitals there are facilities for G.P.s to have their own investigations carried out in the X-ray and pathology departments, and the proportion of these hospitals with such facilities is on the increase? Would it really be such a good thing for all G.P.s to look after all their patients in all hospitals in the whole country? Is it not the main function of the family doctor to be a specialist in family care and domiciliary medicine? Would it not lead to chaos to have a multitude of doctors looking after patients in hospital wards?

His implications that the *standards* of general practice in Britain are lower than elsewhere need careful note and strong rejection. Has he compared the good British G.P. with the good foreign one and also the bad with bad? If so, let us by all means see his findings and the evidence on which they are based. Without any such evidence neither I nor any of my colleagues can accept his implications.

Coming to his suggestions for *improvements* I cannot see how a fee-for-service scheme of remuneration will solve any of the faults he mentions. Would it make any difference to the bad practice, the utility practitioner, or the hospitalisation of medicine? Such a scheme could not of itself necessarily improve standards. He should also realise the very great

advantages of the present capitation scheme, for which a fee-for-service could not easily compensate.

We would all agree that there is room for improvements in our own, and in all, schemes of medical care, all over the world. Personally, I feel that improvements should be based on further studies in general practice to define the problems and their solutions. Our aims should be to decide on some simple and practical methods of assessing standards of medical care; to introduce some more realistic incentives into our methods of remuneration; to introduce some agreeable measures of control to see that suitable standards are maintained; to integrate our medical services and to bring about a better spirit of cooperation with a more active leadership; and to reintroduce a more philosophic attitude to medicine rather than the business one of today.

Beckenham, Kent. JOHN FRY.

SIR,—Your two special articles of May 16, Cost of Prescribing (p. 1035) and Murder at the Cross-roads (p. 1039), make truly gloomy reading. If the capitation system has murdered general practice, then the Hinchliffe Committee has hanged, drawn, and quartered it.

I refer to their statement:

"The Minister should consult the British Medical Association with a view to tightening the present standards for the investigation of instances of excessive prescribing. Where a general practitioner's costs habitually exceed the local average by more than 50% the case should be referred for investigation by the local medical committee. The penalties for excessive prescribing, particularly where doctors prescribe extravagantly in order to attract patients, should be severe."

This means that if a G.P. spends 50% more on his prescriptions than the "average" G.P. in his county, he is hauled before a "Star Chamber" and fined a sum rather more than a child assaulter or drunken driver.

It means that the G.P. returning from his holiday, and finding all his patients waiting for him, will have to palm them off with coloured water, in case the month he returns is the month the Ministry decide to "average out" the cost of his prescribing.

It catalyses the transformation of "home diseases" into "hospital diseases" mentioned by Dr. Geiringer. The corticosteroid in postoperative replacement therapy, the broad-spectrum antibiotic for the atypical pneumonia, must now at all costs be obtained from the hospital pharmacy, and not written on the G.P.'s prescription pad, for fear of reaching the fatal 50% above the average.

As a member of the Surrey Local Medical Committee for the past $10\frac{1}{2}$ years, whose duties have been to inspect surgeries and witness some of these "prescribing investigations", I now feel more like a member of the Secret Police than even a "utility practitioner".

Caterham, Surrey. D. S. PORTER.

SIR,—I could not agree more with what Dr. Sanders (May 23) has to say in reply to Dr. Geiringer's question "Is general practice really necessary?" As year succeeds year the medical training of future G.P.s in Britain becomes increasingly unrealistic. As Dr. Sanders says, "Doctors are trained to deal with situations that are becoming scarce in general practice."

What attempt are the medical schools of this country making to train their students to understand those clinical problems of a psychiatric nature which will bulk so large in their future practices? In my experience lip service is invariably paid from time to time to the existence of these problems by clinical teachers; but there the matter rests; and how can it, in fact, proceed further when the majority of clinical teachers have had no experience of general practice. Time and again senior colleagues have told me how they regretted never having done any general practice. The gulf that has been fixed in the profession between hospital doctors and general practitioners is primarily responsible for this problem. The hospital physician's interests lie with the more recherché aspects of disease, such as disordered biochemistry, pulmonary-artery pressures, and electrolytic homœostasis, especially in teaching hospitals. He must be excused if he, not unnaturally, expects his students to know something of these matters. The general practitioner's work lies far removed from this scientific medical sphere, but no-one is really interested to know whether the student is able to grasp the ætiology of an anxiety or depressive state or grapple with a problem of chronic organ neurosis.

Addition to the overburdened student curriculum of a brief insight into the work of a G.P. is no real answer to the problem and does little to dispel the sense of frustration of the young general practitioner when he finds himself face to face with problems of psychotherapy instead of the "proper" clinical medicine he has been taught to expect.

The statement that "radical revision of medical education is long overdue" has already become a wellworn cliché. Surely though it is an anachronism that in the medical student's crowded final year, proportionately less time is allocated to the study of skin, E.N.T., and eye diseases (which are to bulk so large in his future work as a G.P.) than in his first year to the study of inflorescences of flowers—while little or no attempt is made to acquaint him with the problems of psychological stress in human beings which are to be a major concern throughout the rest of his professional life.

Dundee. EDMUND J. RAFFLE.

SIR,—I had hoped that Dr. Geiringer's reflective article would have produced many replies from much abler pens than mine and was grieved to see that all it produced was a profession of specialisation in psychotherapy by Dr. Sanders last week.

Dr. Geiringer has obviously spent considerable time and thought on his epexegesis but equally obviously he has little concept of what is the nature of good general practice in this country. General practice is what you make it and Dr. Geiringer's "utility" practitioner would soon need the services of Dr. Sanders, and it would serve them both right.

All over this country there are groups of sound intelligent family doctors, working in partnership, each with a pet specialty, perhaps with a hospital appointment, consulting each other on their patients, limiting their lists voluntarily for the good of their patients, with open access to hospital radiology and pathology departments and perhaps their own cottage hospital or maternity units, not hesitating to meet consultants on an equal footing on domiciliary consultation or to refer a problem to hospital for advice, doing their own psychotherapy, attending postgraduate courses regularly, and still finding time to take their rightful share of medical political life. These are the good doctors of the country and they look on their patients as their friends, and their patients feel the same way about them. In them is the renaissance of general practice. If Dr. Geiringer wishes to find them, he has only to become an associate of the College of General Practitioners and he will meet them in abundance among its members. The system of payment makes no difference to such men. They do good work regardless of their pay or fees. As general practice, aided by the college, comes into its own again, the patients of Dr. Geiringer's utility doctor will forsake him, as they can without detriment to themselves under the capitation system of payment, and leave him lamenting.

Dr. Sanders believes there are only two kinds of doctoring—that concerned with repair to the body of damage done by infection, trauma, &c., which will be carried on in hospitals, and that concerned with personality problems, which will be the preoccupation of G.P.s. Heaven forbid that the seminars at the Tavistock Clinic teach such a wretched and meagre

philosophy! Does he really mean that it takes all the paraphernalia of a hospital to treat pneumonia, bronchitis, asthma, the terminal stages of cancer and heart-disease, septicæmias, piles, gastric ulcers, and so on? If so, his patients had better go to Dr. Geiringer!

The job of the family doctor is to treat the whole man, both his psyche and his soma, to help him on his way and advise him in sickness *and* in health, to guide him through all the vicissitudes of his life and help him both on his arrival and his departure. There is but one true form of medicine—family doctoring—and everything else stems from it. I myself believe the good family doctors of this country are second to none.

Reading. W. G. TAIT.

DOCTOR AND FACTORY

SIR,—Both sides of industry, to an increasing extent, want medical services; and whether or not they are fully conscious of the benefits to be gained from the preventive aspects of such services, employers and workers are agreed in demanding primarily a treatment service. Lord Taylor (May 2) believes that this is the foundation on which new industrial medical services should be built; you appear to support him, and so will the vast majority of doctors with experience of work in industry. I have no wish to join issue with Dr. Keatinge (May 9), who is quite happy with "clinical medicine applied to industry" but cannot accept the contention that a large part of industrial medicine is general practice—this is purely a matter of definition. He does not believe the industrial physician should encroach on the field of the general practitioner; but how is that field defined, and is it the same today as it was, say, fifty years ago?

The plain fact is that industry is developing its own health services, and this process is going to continue. Where such facilities are provided at work, a great many functions normally thought of as part of the general practitioner's field are in fact undertaken by the industrial physician, to the satisfaction of all parties, including the G.P. Treatment is not solely, or even principally, a matter of prescribing, and advice and reassurance are themselves therapeutic. Even the rare industrial physician who limited his treatment to this, apart from emergencies, could be held to be encroaching on the field of the general practitioner. But in fact, a large works medical department provides quite considerable therapeutic facilities. The complex process of rehabilitation is essentially therapy in an industrial setting; the majority of skin diseases are, in the considered opinion of many dermatologists, best treated in the works surgery; simple psychotherapy is just as often called for in the factory as in the G.P.'s surgery, and usually more effectively given because more time is available; and treatment of all minor ailments which can be undertaken at work is a commonplace expected by employer and employee.

Too often in the past spokesmen of the medical profession have shown themselves out of touch with changing social patterns affecting the day-to-day practice of medicine. In industrial medicine, this is exemplified by the so-called Ethical Rules for Industrial Medical Officers drawn up by the B.M.A. which are in their present form offensive to the doctor working in industry and utterly unrealistic and unworkable, especially in the older kind of industrial area mentioned by Dr. Jones (May 9) as typical of industrial Britain. A factory in such an area may contain employees from the lists of scores or even hundreds of different general practitioners, and to obtain the prior consent of the G.P. before undertaking any form of treatment other than first-aid would effectively paralyse the work of its medical department. In fact, of course, the rules are broken daily by almost every full-time industrial medical officer, although as a rule any *significant* information about either diagnosis or treatment is *afterwards* passed on to the general practitioner.

None will deny that the patient's interests call for close liaison between all the doctors through whose hands he may pass, including the doctor at work and the family doctor, and usually this occurs quite naturally through the good sense of both parties. It is not brought about by the B.M.A.'s publication, almost every section of which contains the words "the industrial medical officer *shall not* . . ."—particularly when a great many of the things he is forbidden to do are precisely the things which his employers and patients require of him. The B.M.A.'s Central Ethical Committee has strenuously resisted all proposals to bring the Rules more into line with present-day reality, and indeed has recently proposed an amendment of one rule, which, if accepted, would forbid the industrial medical officer to refer a patient for a chest X-ray or blood-count as an aid to the diagnosis of occupational disease or as part of a pre-employment examination. It has also taken the view that industrial medical officers should not carry out poliomyelitis vaccinations (although overruled in this by the General Medical Services Committee) or be sent reports of abnormal findings at mass miniature radiography, even with the patient's consent. The impression given is one of opposition to every development of the work of the industrial medical officer in what are mistakenly conceived to be the interests of the general practitioner. In this somewhat squalid tussle, the wider issue of community health is completely lost sight of.

There is abundant evidence that this attitude is not shared by the average G.P., who welcomes the provision of treatment facilities at the place of work and professional contact with the full-time industrial medical officer, and who will to an increasing extent enjoy opportunities of part-time work in industry as services on the Harlow pattern develop.

Events will force a change of official attitude in the course of time. "Eppur' si muove", Galileo is alleged to have said—and whether he said it or not, history did. But meanwhile it is a pity that industrial physicians of integrity should be put in a position where a great deal of their daily work is, by the standards of their professional organisation, "unethical".

West Midlands Gas Board, Birmingham. F. H. TYRER Chief Medical Officer.

STEROID THERAPY AND PEPTIC ULCERATION

SIR,—In your leading article of April 4 you refer to "that bugbear of all steroid therapy—the development of peptic ulceration". At this centre our anxiety on this score has been greatly reduced during the past eighteen months by the use of enteric-coated prednisolone tablets.

There were two main reasons for using such tablets: (1) Cortisol and its presently used analogues are potent anti-inflammatory agents when applied locally, so that the presence of relatively high concentrations in the stomach will not favour the healing of injuries to the mucosa or ulcers; (2) the parenteral administration of cortisol, as by controlled corticotrophin (A.C.T.H.) therapy, is rarely accompanied by dyspepsia. (Excessive doses may cause abdominal distension.) Our own experience is of some 70–80 patient-years of corticotrophin therapy.

It took us some six months to procure an enteric-coated tablet of prednisolone that would dissolve sufficiently quickly in the small intestine to avoid bacterial degradation and inactivation. Since then, during the last eighteen months, we have transferred 20 patients who had dyspepsia or a known peptic ulcer from plain to coated prednisolone tablets. The doses have varied from 7·5 to 12·5 mg. for patients with

uncomplicated rheumatoid arthritis and have been as high as 60 mg. for patients with polyarteritis nodosa. All the patients have claimed that their dyspeptic symptoms were lessened and none has bled from an ulcer or perforated. As all the patients have taken analgesic tablets, as well as prednisolone, it was not to be expected that they would all lose their dyspepsia.

The only contraindication to using enteric-coated prednisolone tablets is intestinal hurry. This minor alteration to therapy is worth adopting.

Thanks are due to Dr. F. R. Fletcher, of Pfizer Ltd., for having the prednisolone tablets enteric-coated and for an unlimited supply of the tablets for eighteen months.

Nether Edge Hospital, Sheffield. HARRY F. WEST.

PHYSICAL CHANGES IN THE PROLAPSED DISC

SIR,—I have followed with interest the discussion [1–5] on this subject. Some basic data are known [6–8] but there are still many unsolved problems.

In the biomechanical laboratory of this department I have developed a method for measuring pressure within the disc.[9] Because of the properties of the nuclear substance it is impossible to measure this pressure via an open needle. But if the nuclear substance is acting on an elastic membrane which in its turn acts on a mechano-electrical pressure transducer, reliable and comparable values can be obtained. The elastic membrane consists of polyethylene tubing (PE 90) which is threaded over a Luer-Lok needle. The needle-end is plugged and a small hole (3 × 1 mm.) is made in its side. The hole is covered by the membrane. The needle is inserted into the nucleus of the disc. The pressure transducer is of the Kifa-Elema type which is used in ordinary intracardiac pressure measurements.

Experiments were made on about 100 fresh lumbar intervertebral discs, taken at necropsy. The discs were loaded vertically in a compression apparatus with loads ranging from 402 to 20 kg. Each disc was subjected to loading between half of the upper and lower adjacent vertebræ. The position of the pressure-sensitive membrane in the nucleus was controlled by X-ray films in two planes.

With this method it is possible to *prove* that the nucleus pulposus has true hydromechanic properties. Moreover, it is shown that the nuclear substance keeps these properties during ageing, in spite of the fact that severe degenerative changes were found in some of the specimens.

To get a clear picture of the pressure within the disc as well as to compare the results with different specimens, the area of the disc must be carefully considered.

After cross-sectioning the discs, the area was determined with an Amsler planimeter. The pressure in the nucleus is measured in kg. per sq. cm., and by dividing this figure with the stress in kg. per sq. cm. to which the disc is subjected a quotient called the pressure index is obtained. At the same time this index is a measure of the weightbearing capacity of the nucleus. Average pressure values are lower for degenerated discs (i.e., discs showing annulus ruptures and gross anatomical nuclear changes) than for normal discs. The weightbearing capacity in a normal L4 disc is on an average 50% greater than that of a degenerated L4 disc. Fracture of an endplate decreases the intradiscal pressure by 30–40%. When the arches and intervertebral joints are removed the pressure does not increase by more than 10–20%, and there is no great difference in this respect between normal and degenerated discs. If the discs are immersed for twenty-four hours in distilled water or physiological saline solution no significant change in intradiscal pressure can be registered when the discs are subjected to repeated loading.

The relation between the total pressure transmitted by the annulus and that transmitted by the nucleus may be calculated for various indices and different surface areas of the nucleus, according to the following formula:

$$\frac{P_a}{P_n} = \frac{1 - \frac{A_n}{A_d} \quad I}{I\left(1 - \frac{A_n}{A_d}\right)}$$

$$I = \text{Index} = \frac{P_n}{P/A_d}$$

where P = force applied to whole disc
P_n = ,, transmitted by nucleus
P_a = ,, ,, ,, annulus
A_d = disc area, A_n = nuclear area

With the Amsler planimeter it was calculated that the nuclear surface area constitutes on an average 60% of the total surface area of the disc. A lowering of the pressure index from 1·5 to 1·0 will, according to the above formula, imply a four times greater stress on the various parts of the annulus. This may conceivably be the reason why the annulus ruptures.

Orthopædic Department,
Royal Academic Hospital,
Uppsala, Sweden. ALF NACHEMSON.

CARDBOARD BOXES IN OPERATING-THEATRES

SIR,—The appendix on cardboard boxes in the Nuffield Provincial Hospitals Trust report on Present Sterilisation Practice in Six Hospitals has prompted me to examine bacteriologically the cardboard containers of certain packs that are used in operating-theatres.

All specimens of cardboard examined have yielded viable spores of the genus clostridium, frequently two or more species. *Clostridium sporogenes* has always been present. So far I have failed to isolate *Cl. tetani*, but I feel that this is probably fortuitous.

Certain packs contain sterile apparatus ready for immediate use (e.g., disposable transfusion sets), and these packs are often sealed in such a way that they have to be cut or torn open in operating-theatres in the presence of patients with exposed wounds. It seems to me that this practice entails an unnecessary risk, however small, to the patient, of introducing dangerous organisms into the wound.

This risk would be eliminated if the manufacturers could be persuaded to abandon cardboard, and to package their products in plastic or other bacteriologically acceptable material. Meanwhile I suggest that wherever possible cardboard packs are kept out of operating-theatres, and that they be opened, when essential, with the greatest care to prevent the dissemination of spores.

Bland-Sutton Institute of Pathology,
Middlesex Hospital, London, W.1. R. E. M. THOMPSON.

DOCTOR OLIVER GOLDSMITH?

SIR,—In your review of Dr. Hugh Barber's attractive book, *The Rewards of Medicine*, you ask, "did not Oliver Goldsmith hold a medical degree?". The answer was given by Raymond Crawfurd [1] in a forgotten paper which is not even read by Goldsmith's biographers.

Crawfurd showed that there is no evidence for a medical degree either in Dublin or the Continent, and in a shy footnote suggests that the Oxford M.B. of 1769 *ad eundem gradum* may have been a hoax arranged by Goldsmith himself.

The 18th century was, while realistic concerning the vagaries of human personality, more tolerant than we are of the eccentricities of genius—and Goldsmith's false pretences were shrugged off with a laugh. It is strange that the evidence for the M.B. or the M.D. should not have been critically examined by biographers, for the facts confirm the interpretation of Goldsmith's complicated personality made by Boswell, by Johnson, and by Joshua Reynolds.

The Children's Hospital,
Edgbaston, Birmingham. DOUGLAS HUBBLE.

1. *Proc. R. Soc. Med.* 1914, **8**, 7.

1. *Lancet*, 1958, i, 1214.
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3. Hendry, N. G. C. *ibid.* p. 158.
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7. Hirsch, C., Paulson, S., Sylvén, B., Snellman, O. *ibid.* 1952, **22**, 175.
8. Petter, C. *J. Bone Jt Surg.* 1933, **31**, 365.
9. Nachemson, A. Meeting of Scandinavian Orthopædic Association, September, 1958. *Acta orthop. Scand.* (in the press).

CAUSE OF CLUBBING

SIR,—Dr. Leslie Doyle (May 9) offers an ingenious explanation of the fluctuating œdema sometimes observed in hypertrophic pulmonary osteoarthropathy.

I look forward with much interest to the experimental testing of his hypothesis. Meanwhile, it should be remembered that ferritin (which I believe to be responsible for the circulatory changes found in clubbed fingers) is a potent antidiuretic substance.[1] Periods of fluid retention could then be accounted for by increased quantities of ferritin being shunted past normal lung tissue. As far as I know, no mineral and water balance studies have been carried out on patients with osteoarthropathy. I am sure they would give much valuable information.

A recent paper by Pierce et al.[2] throws light on an associated problem—the occasional development of clubbing in liver disease. It seems that venous admixture can be demonstrated in the arterial blood of such cases. This may be brought about by the development of pulmonary arteriovenous fistulas (possibly by the same cause as that responsible for spider angiomata in the skin), or shunting of blood from the high-pressure portal-vein radicles into the low-pressure pulmonary-vein branches.

At the risk of a charge of heaping Ossa on Pelion, I would again point out how this fact supports the view that it is the shunting of blood past the lung which is responsible for clubbing.

Royal Devon and Exeter Hospital, Exeter. G. H. HALL.

THE PROTRUDED DISC

SIR,—I have recently had the opportunity of meeting Dr. George S. Jackett, of Ohio, who introduced to me the conception of relaxation of the ligaments, especially the iliolumbar and sacroiliacs, in cases of low backache and sciatica. The pain in these cases is usually referred and sometimes due to direct irritation of the sciatic nerve as it leaves the pelvis and can often be relieved by treating these ligaments.

Dr. Hackett treats this relaxation by injection into the ligament of a proliferating and sclerosing solution, with a view to encouraging fibrosis and so tightening the ligament and at the same time relieving the pain.

Although I have been treating patients along Dr. Hackett's lines for only a short time, my results have been such as to convince me that in backache and sciatica it is well worth treating them by this method, and I feel it should be given a trial before laminectomy is performed and often after laminectomy has failed.

I do not think it is realised what a large part sacroiliac relaxation plays in cases thought to be due to disc protrusion.

Doncaster. W. MCCAUSLAND SCOTT.

SIR,—Your annotation of May 19 on present-day treatment of the disc lesion was of special interest to me.

I should like to advance a new theory about the probable cause, which might enable surgical interference to be avoided.

My experience suggests that a large number of disc lesions—especially in the younger and middle age-groups—are often secondary to primary lesions in the lumbosacral and sacroiliac joints, caused by heavy falls, " strains ", and other trauma. Even a slight strain of a sacroiliac joint may result in a degree of subluxation that will cause recurrent attacks of lumbar or sciatic pain over a period of years unless it is corrected by manipulation.

Often it will be found on X-ray examination that, associated with these lesions in the lumbar region, there is torsion of the lumbar spine. If the initial lesion is not corrected by manipulation the following chain of events may ensue:

The torsion of the spine is not relieved. Faulty posture continues. One or more intervertebral discs become compressed laterally on the affected side. This mechanical compression per se or the subsequent fibrosis in the nucleus pulposus could, in my opinion, give rise to the classical signs of the disc syndrome. A sudden bending or a twist or a fall could then bring on the acute attack that immobilises the patient.

X-ray examination may show diminution of the intervertebral spaces but the primary cause—the lesions of the lumbosacral and sacroiliac joints—are often missed or their importance not sufficiently appreciated.

Excellent results have been achieved in cases of disc lesion by concentrating all treatment by manipulation and massage on the primary lesions, should they be present.

London, W.1. LOUIS MOSS.

MEDICAL CONSPIRACIES?

SIR,—A member of the public who pays (whether out of his own pocket or through the Exchequer) for professional advice does so in the belief that the advice and any action taken in regard thereto will be authoritative and performed with skill, and that, if there is any defect in the advice or action taken, a remedy will be available against the member of the profession.

In any proceedings which a member of the public may take claiming damages for negligence against a solicitor, architect, or accountant, it will be found that the other members of the profession concerned are willing to give their advice in respect of such litigation quite dispassionately and without concern for the fact that the defendant is a brother in the same profession. This state of affairs is to be applauded.

Unhappily, the same does not seem to be so in the medical profession, where almost all members will attempt to persuade the injured patient not to pursue his remedy in law. In my experience the assistance which one doctor is prepared to give another includes the following:

Refusing to make any statement as to what occurred in an operating-theatre until actually subpœnaed and giving evidence in court. This refusal is a very serious deterrent to a prospective litigant, who will not know what the doctor's evidence is going to be.

Communicating to the prospective defendant the result of an examination made at the expense of the litigant. The defendant doctor or surgeon is then thoroughly aware of all matters pertaining to the prospective litigant's condition.

Advising the litigant that the negligence may very well be held to be in the class of " dismissible accidents ", so as to encourage the dropping of proceedings.

Refusing to deliver up an independent specialist's report to one's own patient to be used in assisting in the presentation of the plaintiff's case.

Refusing to give treatment to a person who is suing another doctor for damages for negligence.

The effect is, of course, to induce a state of mind in the litigant which will save the defendant much embarrassment and possibly heavy damages.

Almost all doctors are members of one of the defence organisations, and, whether by reason of such additional bonds of brotherhood or otherwise, there is a cloak of conspiracy around the whole profession designed to deprive the injured patient of any remedy.

The inference to be drawn is that the medical profession places no trust in the competence of British justice to relieve it of responsibility if it is right that it should be so relieved.

In my opinion a directive should be addressed to all doctors advising them that their duty as citizens to assist persons who are entitled to call upon their services

1. Shorr, E. *Harvey Lect.* 1954–55, series 50, 112.
2. Pierce, J. A., Reagon, W. P., Kimbell, R. W. *New Engl. J. Med.* 1959, **260**, 901.

as witnesses or otherwise in proceedings against other doctors takes precedence over the duties which they may owe to other members of the medical profession by virtue of the brotherhood existing between members of the same profession.

London, W.11. CYRIL BEACH.

TRAUMA AND SQUAMOUS SKIN CANCER

SIR,—Dr. Bray's account (April 25) of an epithelioma healing completely after excision with a penknife is very interesting. The tumour arising on the skin over the facial region, history of a thorn prick, clinical resemblance to typical ulcerating epithelioma, and cure with rather minimal treatment suggest the possibility of keratoacanthoma rather than squamous-cell carcinoma.

This entity is not too well recognised and is often confused with squamous-cell carcinoma of the skin. The histological picture is usually characteristic though the differentiation from squamous-cell carcinoma may be difficult in some cases. The nature and ætiology of keratoacanthoma are yet unknown. Very often these tumours regress spontaneously in a few weeks. If one prefers to treat them, local surgical excision, destruction with electrocoagulation, or X-radiation are the three methods available.

Roswell Park Memorial Institute, Buffalo, New York. ARVIND Y. LONKAR.

DEFIBRINATION SYNDROME IN PREGNANCY

SIR,—I read with great interest the letter by Professor Jeffcoate and Mr. Scott (Feb. 7) as well as the article by Sharp et al.[1]

During the past few years I have been studying the properties of incubated lysed fibrinogen, and some of my findings may help to explain the observation of your contributors—namely, that while the prolonged thrombin-time of some patients suffering from obstetrical hypofibrinogenæmia seems to suggest a lowered concentration of fibrinogen, chemical methods fail to substantiate any important decrease in the clottable protein. Sharp et al. suggest that this phenomenon is due more likely to altered reactivity of fibrinogen than to the presence of an anticoagulant, because they observed that addition of the patient's plasma to normal plasma does not prolong the thrombin-time of the latter.

We have shown [2 3] that the fraction of incubated fibrinogen precipitated between 25% and 50% ammonium-sulphate saturation possesses anticoagulant properties. This anticoagulant fraction of incubated fibrinogen (A.F.I.F), when added to freshly drawn blood, prevents coagulation. The required concentration expressed as tyrosine was found to be 46 ± 17 mg. per 100 ml. plasma-fibrinogen mixture. This effect can be reversed by approximately fivefold dilution with distilled water and addition of calcium chloride or thrombin, thus excluding fibrinolysis as the cause of the anticoagulant effect. Biochemical determinations of the fibrinogen content of blood rendered unclottable by A.F.I.F. showed it to be within normal limits. In impressive resemblance to the findings of Sharp et al. and Jeffcoate and Scott the thrombin-time of the plasma of the same blood was infinity. Thrombin, however, although its action is completely inhibited, is not destroyed by A.F.I.F., even when incubated with the anticoagulant. By a Lineweaver-Burk plot, we showed that the antithrombin activity of A.F.I.F. is competitive in nature.[4] In striking analogy with what happens in obstetrical hypofibrinogenæmia,[1 5] we found that the concentrations of factor V and plasma precursors of plasma thromboplastin are decreased in blood rendered uncoagulable by the addition of A.F.I.F. On the other hand, the concentrations of prothrombin, factor VII, and serum precursors of plasma thromboplastin and fibrinogen remained normal.

In work still in progress we found that fibrin clots prepared from Laki's fibrinogen,[6] as well as clots prepared from human plasma by addition of thrombin, dissolve after 24–48 hours' incubation and that the fraction precipitated between 25% and 50% saturation with ammonium sulphate prevents completely the coagulation of shed blood. What is particularly interesting, however, was the fact that if A.F.I.F. prepared from fibrin is added to citrated plasma in amounts less than those required to prevent clotting of native plasma, coagulation occurred. This can be explained by the well-known fact that fibrin adsorbs thrombin, which becomes released upon lysis of the clot. We think that this observation may offer an explanation of the failure of Sharp et al. to notice a prolongation of the thrombin-time of normal plasma on addition of the patient's plasma. What may have happened is that, after intravascular clotting, the fibrin formed was lysed with subsequent release of thrombin together with the lysed fibrin. If the test was performed before the neutralisation of thrombin by the natural antithrombin, thrombin may have covered the anticoagulant action of lysed fibrin. Taking this syllogism in reverse, one may speculate that the main function of lysed fibrin is to inhibit the action of the thrombin released during fibrinolysis, until antithrombin has had time to neutralise thrombin.

The resemblance of our in-vitro findings with lysed fibrinogen and lysed fibrin to those found in obstetrical hypofibrinogenæmia suggests that the coagulation abnormalities of the latter are due to intravascular clotting with subsequent lysis of the formed fibrin deposits and formation of an anticoagulant identical or similar to A.F.I.F.

Department of Physiology and Pharmacology, University of Alberta, Edmonton, Alberta. D. C. TRIANTAPHYLLOPOULOS.

ADRENAL HÆMORRHAGE IN INSULIN SHOCK

SIR,—Cortisone-treated rabbits proved to be strongly resistant to insulin shock.[7] Repeated administration of insulin 3–10 days after stopping the hormone treatment was followed by a severe insulin shock.

Its severity was shown by the fact that in 6 cases out of 30 an immediate intravenous injection of glucose solution failed to bring the shock to an end and the animals died.

In 4 of the 6 animals unilateral bleeding and necrosis of the adrenal gland was demonstrated and proved by histological findings.

According to the fasting blood-sugar values, though stopping cortisone was followed for a time by an increased glycogenesis in the liver, the shock-preventing action of cortisone had ended and the susceptibility to shock was increased. This susceptibility was obviously further increased by the insulin-induced adrenal hæmorrhage and necrosis. It is striking that in cases with an adrenal lesion (proved histologically) the hypoglycæmic shock, accompanied by the characteristic attacks of spasm, developed at a relatively high blood-sugar level (see table).

Animal	Cortisone		Change in blood-sugar level in response to insulin	
	Period of treatment	Dose per day	During cortisone	After cortisone
1	10 days	15 mg.	146 mg.–56 mg.*	266 mg.–84 mg.
2	9 days	15 mg.	132 mg.–40 mg.	102 mg.–60 mg.
3	8 days	15 mg.	228 mg.–66 mg.	114 mg.–60 mg.
4	6 days	20 mg.	—	130 mg.–66 mg.

* The first value is the initial level of the fasting blood-sugar and the second is the lowest recorded. The second value after cortisone is the level observed when the hypoglycæmic attack developed.

Cortisone thus protects against the development of insulin shock, whereas the rapid formation of adrenal lesions may aggravate the insulin shock. The fact that

1. Sharp, A. A., Howie, B., Biggs, R., Methuen, D. T. *Lancet*, 1958, ii, 1309.
2. Triantaphyllopoulos, D. C. Proceedings of the 11th Meeting of the Western Regional Group of the National Research Council of Canada, January, 1957. Banff, Alberta.
3. Triantaphyllopoulos, D. C. *Canad. J. Biochem. Physiol.* 1958, **36**, 249.
4. Triantaphyllopoulos, D. C. *Fed. Proc.* 1959, **18**, 161.
5. Greenwalt, T. J., Triantaphyllopoulos, D. C. *Amer. J. clin. Path.* 1955, **45**, 135.
6. Laki, K. *Arch. biochem. biophys.* 1951, **32**, 317.
7. Barta, L., Simon, G. *Lancet*, 1957, ii, 885.

insulin shock developed in our cases at a relatively high blood-sugar level may be connected with the development of adrenal hypofunction.

1st Department of Pædiatrics,
2nd Institute of Pathological Anatomy,
University Medical School, Budapest.

L. BARTA
E. BEREGI
H. JELLINEK.

POLYCYTHÆMIA

SIR,—Your well-written leading article of April 18 mentions the life-span of the red cell, which, according to most information, seems to be normal. One of the first, probably *the* first, to point this out was Merskey [1], using the Ashby technique.

In 1950 I had the opportunity to perform 5 cross-transfusions from a patient with polycythæmia vera 24, 44, 110, and 290 days after treatment by radioactive phosphorus. The life-span was about 3 times shorter than normal during the last 3, and still shorter during the 1st cross-transfusion. Even if this short span was due to previous treatment, I am reluctant to believe that a normal life-span has been definitely proved in this disorder. The increased iron-turnover noted by Lapage and Lawrence, and the results of Berlin et al. are contradictory. I believe there is still some work to be done to solve this tricky problem.

St. Josephs Hospital,
Porsgrunn, Norway. A. SCHRUMPF.

ANTIBIOTIC COMBINATIONS

SIR,—We were pleased to read Dr. Sales' letter of May 9 criticising our clinical trial of 'Albamycin T'. We were, however, surprised that he should condemn our motives and results at this early stage. Our letter on the subject was, after all, an interim report, and we who are conducting the trial do not yet draw any definite conclusions.

We should like to point out that we are making an honest attempt to evaluate the claims made by the manufacturers of albamycin T on behalf of their preparation.

Dr. Sales is willing to assume that albamycin T will shortly join the ranks of ineffective antibiotic preparations against staphylococcal diseases, yet our results to date suggest that this may not come to pass. The rapid responses obtained with albamycin T indicate that the emergence of resistant strains may be minimised.

In our cases so far, the incidence of side-effects has been very low indeed and no skin rashes have been reported. We thus can in no way confirm Dr. Sales' statement that novobiocin is the frequent cause of sensitivity reactions.

As we originally stated, it is our intention to build up a large series of cases, after which we shall submit a final report. We then hope to draw some useful and instructive conclusions.

R. A. MCGREGOR
S. A. PRICE
M. MCK. SHAW
R. HIGH
F. J. BIRKETT
F. A. BREAR
J. P. SHACKLETON
I. J. WAITE
A. J. WALEWSKI.

SIR,—Dr. Hicks' protestations (May 16) that sensitivity reactions to novobiocin are small in number are too late, for the fact that this is not so has even been recorded in a standard textbook of medicine.[2]

The article by Dr. Buhr and Mr. Scott (May 16) also confirms my statement that there is a rising incidence of tetracycline-resistant staphylococci amongst the general public. With this situation as an accomplished fact, the use of 'Albamycin-T' as recommended can only succeed in treating infections due to this organism with sub-therapeutic doses of novobiocin. This is an assured way of breeding a resistant strain, possibly even more virulent and difficult to control. I might add that I am not objecting to the proper use of novobiocin, or of suitable combinations of antibiotics where the occasion demands, but the use of albamycin-T as a panacea appears unjustifiable.

Rhoose, Glamorgan. NORMAN SALES.

1. *S. Afr. J. med. Sci.* 1949, **14**, 1.
2. The Principles and Practice of Medicine (edited by Sir Stanley Davidson). Edinburgh, 1958.

POTASSIUM LOSS DURING TREATMENT WITH CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE

SIR,—Your leading article of April 11 stated that there seems to be no difference between chlorothiazide and hydrochlorothiazide in regard to their effects on potassium excretion. According to our observations, the danger of potassium loss is considerably less after hydrochlorothiazide than after chlorothiazide.

We have been using hydrochlorothiazide since September, 1958, in more than 100 patients with various œdematous disorders. Bioassay studies [1 2] using sodium excretion as a parameter, as well as clinical experience,[3] have shown that hydrochlorothiazide is about 20 times as potent as chlorothiazide. In controlled experiments (electrolyte balance) several differences in the mode of action of these two diuretic agents were noted.[2] Hydrochlorothiazide does not produce an increase in bicarbonate excretion and urinary pH such as occurs after chlorothiazide. Chlorothiazide produces a mixed sodium—potassium and chloride—bicarbonate diuresis while hydrochlorothiazide only increases excretion of sodium and chloride (similar to mercurial diuretics). Compared with chlorothiazide the onset of action after oral hydrochlorothiazide is delayed (4–6 hours) while its action lasts longer (up to 24 hours).

The most important difference between the two drugs was concerned with potassium excretion. In the same series of patients no increase in potassium excretion was noted after 25 to 75 mg. of hydrochlorothiazide while a significant increase followed 2000 mg. of chlorothiazide. Studies of electrolyte excretion in patients with acute congestive heart-failure and œdema corroborated these observations. In no case did potassium excretion increase above intake, though all patients had a considerable diuresis with much loss of sodium and body-weight.[3] Analysis of serum-electrolytes reflected the different mode of action of the two drugs. After chlorothiazide a drop in serum-potassium is often observed while serum-chloride concentration usually stays within normal limits. Hydrochlorothiazide leads almost regularly to a hypochloræmia (90–100 mEq. per litre) while potassium rarely is depressed.

These observations on the quantitative and qualitative differences between the two drugs have been corroborated by Ford [4] in the U.S.A. and Losse et al.[5] in Germany. The contradictory results of Moyer et al.[6] are easily explained. They used doses up to 2000 mg. of hydrochlorothiazide (i.e., 100 times the average therapeutic dose). It should be noted that most cardiac patients do not need more than 12·5–25 mg. of hydrochlorothiazide for satisfactory diuretic effect. In more resistant cases the dose has to be increased to 100 or even 150 mg. per day or the drug has to be given intramuscularly. It should be stressed that hypopotassæmia may occur after hydrochlorothiazide (as it may after any diuretic). This should be expected and prevented (1) whenever high doses of hydrochlorothiazide (more than 75 mg. per day) are used over prolonged periods of time and (2) in conditions with a spontaneous trend to potassium loss (e.g.,

1. Richterich, R. *Experientia*, 1958, **14**, 458.
2. Richterich, R. *Klin. Wschr.* 1959, **37**, 355.
3. Richterich, R., Spring, P., Thönen, H. *Schweiz. med. Wschr.* 1959, **89**, 353.
4. Ford, R. V. *South. med. J.* 1959, **52**, 40.
5. Losse, H., et al. *Münch. med. Wschr.* 1959, **101**, 677.
6. Moyer, J. H., et al. *Amer. J. Cardiol.* 1959, **3**, 113.

diarrhœa, vomiting, steroid treatment, cirrhosis of the liver). Nevertheless, hydrochlorothiazide, in our opinion, represents another step towards the development of the "ideal diuretic".

Medizinische Universitätsklinik,
Basle, Switzerland. R. RICHTERICH.

INFANTILE SPASMS AND HYPSARRHYTHMIA

SIR,—We were interested in the report by Dr. Cox and Dr. Martin (May 23) of improvement in a patient with infantile spasms when treated with corticosteroids. Since writing our paper of March 21 we have treated 7 such children with corticotrophin and, as a result of this experience, we agree with them that hormone treatment should be tried in all patients with this condition.

Before treatment all our patients were having several spasms daily, their E.E.G.s were either hypsarrhythmic or epileptic, and they were obviously mentally retarded. Corticotrophin was given daily or twice daily in the gel form. The first course lasted a month, and in 4 patients a recurrence of spasms made a second course of a month at higher dosage necessary. The daily dose varied from 5 units for an infant of two months to 25 units for a child of three years. (We now use an initial daily dose of at least 20 units for all ages.) E.E.G.s were taken twice weekly during treatment and, using our scoring system, the degree of abnormality was assessed. This assessment was carried out by P. M. J. with no knowledge of the patient's treatment at the time.

Spasms stopped during the first week in all 7 patients and there was a coincident E.E.G. improvement in 6. At present (one to four months after stopping treatment) the patients' status is as follows:

		No. of patients
Epilepsy	No spasms	5
	Spasms continue	2
E.E.G.	Normal or non-specific abnormality	3
	Improved but still epileptic	3
	Unchanged	1
Mentality	No definite improvement	7

The striking improvement in epilepsy has not been paralleled by mental improvement. Although 3 children have acquired new abilities there has as yet been no increase in the Griffiths development quotient (Dr. B. S. B. Wood). Mental improvement may be dependent upon initiating treatment within a few weeks of the onset of the spasms.[1] Our failure in this respect may therefore be due to lack of the opportunity to treat any patient within the first two months of the disorder. There is clearly a great need for diagnostic awareness at all levels if we are to be given the opportunity to test this hypothesis. Too often the explanation of salaam spasms as "colic" or "trying to sit up" is sustained for several weeks before the correct diagnosis is made.

Although mental retardation is the most serious aspect of the disorder, the prevention of further spasms is obviously a worthwhile result and it appears that success is not so dependent upon early treatment. 1 of our patients whose spasms ceased and whose E.E.G. became normal had had the disorder for eighteen months. Nor, apparently, is corticotrophin only effective in patients whose condition is due to a postnatal cause. A child had a history suggestive of perinatal cerebral insult; labour was difficult, he had blue asphyxia, and mental retardation and a spastic monoparesis dated from birth. Yet he lost his spasms on treatment and his E.E.G. now shows no epileptic phenomena.

Further use of hormone treatment is justified both on humanitarian and scientific grounds. Careful assessment of the results of such treatment not only is necessary for a more precise formulation of its uses but also may lead to new knowledge about the nature of the disorder and even of epileptic phenomena in general.

The Children's Hospital,
Edgbaston, Birmingham. B. D. BOWER
P. M. JEAVONS.

1. Sorel, L., Dusaucy-Bauloye, A. *Acta neurol. belg.* 1958, **58**, 130.

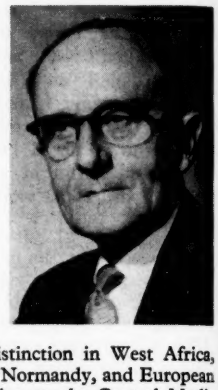
Obituary

BERNARD RICHARD MILLAR JOHNSON

F.R.C.S., F.F.A. R.C.S., D.A.

Dr. Bernard Johnson, consultant anæsthetist to the Middlesex Hospital, died on May 18 at the age of 54.

He was educated at Brighton College, and at the age of 17 he joined the medical school of the Middlesex Hospital, whence he qualified in 1927. After serving there as house-surgeon to Sir Gordon Gordon-Taylor and as casualty surgical officer, he considered specialising in tropical medicine and spent a year abroad. On his return to this country he took up the study of anæsthesia as senior resident anæsthetist at the Middlesex Hospital. He was appointed assistant anæsthetist to the hospital in 1931, and by 1933 he was also anæsthetist to St. Peter's Hospital and to the dental department at University College Hospital. Already adept in endotracheal anæsthesia, he turned his attention to the improvement of dental anæsthesia, and with his colleagues, Sir Robert Macintosh and Dr. W. S. McConnell, developed a first-class service for the administration of dental gases. In 1936 he was appointed to the full staff of the Middlesex Hospital, and four years ago he became senior consultant anæsthetist.



Throughout the late war he served with the R.A.M.C. with distinction in West Africa, the Middle East, and in the Italian, Normandy, and European campaigns. He was anæsthetic advisor to the Central Mediterranean Force and held the rank of lieut.-colonel. He was mentioned in despatches in 1944. After the war he retained his contact with the Services as civilian consultant anæsthetist to the War Office.

The war interrupted many of his activities on behalf of anæsthesia, but he was a member of the council of the Association of Anæsthetists of Great Britain and Ireland in 1943 and its honorary treasurer from 1947 to 1950. He took no small part in the early development of the Faculty of Anæsthetists within the Royal College of Surgeons, and he was a founder member of the board of Faculty and its vice-dean. He was awarded the F.F.A. R.C.S. in 1948. Four years later he became dean of the Faculty and a member of the council of the Royal College of Surgeons, a post which he held for three fruitful years. While he was dean the examination of F.F.A. R.C.S. was instituted and he exerted great influence in designing the framework of the examination and was himself an examiner up to the time of his death. He was elected an hon. F.F.A. R.C.S. in 1953, and immediately after completion of his deanship he became president of the anæsthetic section of the Royal Society of Medicine in 1954–55. He was elected to the fellowship of the Royal College of Surgeons in 1956.

Bernard Johnson's interest in research and the propagation of knowledge in his specialty took many forms. He was responsible for obtaining generous support in the form of endowments and study grants from commercial and industrial interests. He also took a great part in the organisation of Scientific Days at the Royal College which were attended by anæsthetists from all over Great Britain. He travelled widely, lecturing and demonstrating in modern anæsthesia in Australia, France, Germany, Switzerland, and Greece, and he was made an honorary member of the anæsthetists' associations in these countries.

A colleague writes:

"During the pre-war years Bernard Johnson pioneered the introduction of intravenous anæsthesia into Great Britain, and

this illustrates his ability, almost clairvoyant, to know what was of importance for the future of this branch of medicine. More recently this was illustrated by his interest in halothane and his realisation that this non-explosive drug might well be another milestone in anæsthesia. He was particularly interested in anæsthesia for thyroid surgery and for urology, and he contributed much in textbooks on these subjects and on intravenous anæsthesia—articles full of wisdom and knowledge gained from his wide experience. Many other papers published in recent years owe their origin to him, for his penetrating mind suggested numerous subjects for investigation by his juniors, who received his unstinted help and advice in their work. As a teacher he was a fine lecturer, but at his best in practical demonstration and informal discussion.

" At the Middlesex Hospital, B. J. will be sadly missed. His courtesy and charm to all, his careful assessment and skilful management of the patients he anæsthetised, and his insistence on safe anæsthesia performed with the utmost concentration will remain as an example for all who succeed him. He undertook all his extra responsibilities at the Middlesex Hospital cheerfully and with great dedication. He was chairman of the medical committee in 1957 and since then had been a member of the board of governors. He had a wide knowledge of committee procedure and an ability for clear and concise summing up.

" A man of great moral courage and conviction, his opinion was always sound, and the helpful advice and guidance given to colleagues and juniors will be remembered with gratitude. He had a philosophy of life and behaviour that was well suited to a leader of men. He had many outside pursuits. He took a keen interest in sport, particularly cricket, and he was a great countryman and naturalist. His knowledge of wild life, especially of birds, was encyclopædic. He was an accomplished gardener and smallholder, and it was on holiday, in his country home in Sussex, that he died."

Dr. Johnson leaves a widow and daughter.

ARTHUR HARRIS

M.A., M.D. Manc., D.P.M.

Dr. Arthur Harris, physician to Bethlem Royal Hospital and the Maudsley Hospital, London, died in King's College Hospital on May 22, at the age of fifty.

Born and educated in Manchester, he took a degree in economics before turning to medicine. He graduated M.B. in 1934, and after holding various house-appointments decided to specialise in psychiatry. He entered the mental-health service of the London County Council, and held posts at Bexley, Hanwell, St. Francis observation unit, and the Maudsley Hospital. During the late war he served in the R.A.F. Medical Service.

On demobilisation he returned to the staff of the Maudsley Hospital, and after the amalgamation of Bethlem with the Maudsley in 1948 he took an active part in developing the services of the joint hospital. His pioneer work for day-hospitals, which he described in our columns two years ago, was a valuable contribution, not only to his own hospital, but to community care generally.

A. L. writes:

" Arthur Harris had exceptional qualities which were never paraded, and were indeed often half-hidden behind his unassuming manner. With his acute intelligence, his training in economics, and his sound practical judgment he was able to bring to the affairs of the hospital, during the formative changes that came after the war, a breadth of view and grasp of essentials which were invaluable. He gave the hospital unlimited time and devotion: the many years during which he was elected chairman of the medical committee indicated how well his colleagues recognised his integrity and wisdom. He was a man of few words, but everything he said was to the point, shrewd, unequivocal, and full of good sense.

" In his clinical work he speculated little about psychopathology, but drew heavily on his experience, which had been varied, and on his wide and discriminating knowledge of the literature of the subject. He was far-sighted and skilful in adapting the transatlantic idea of a psychiatric day-hospital to meet local needs in this country: his success demonstrated the value of the day-hospital, while characteristically, in his writings and lectures, he set out its limitations as fully as he did its scope and virtues. The combination of innovating energy with a capacity for just appraisal of the defects as well as the merits of a therapeutic procedure is not common, but he showed it conspicuously. It was evident in the successive studies he made of the efficacy of leptazol, carbon dioxide, insulin coma, and other physical treatments. His inquiries, carefully designed and soberly analysed, gave no hint of bias: and they were carried out against a background of equally careful analyses of course and prognosis which he had made from 1938 (when he published an informative survey of what happens to patients with an anxiety state) until recently, when he added to his many papers on the natural history and prognostically important features of schizophrenia.

" Arthur Harris was a man of strong convictions, unselfish, sincere, and single-minded. His untimely death leaves a painful gap in the affection of his friends and deprives English psychiatry of a singularly disinterested, steady, and enlightened exponent."

Diary of the Week

MAY 31 TO JUNE 6

Monday, June 1st

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Emotional Reactions to Physical Illness.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Dr. B. J. Anson (Chicago): Otic Capsule, Perilymphatic Labyrinth, and Periotic Appendages.

Tuesday, 2nd

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. David Hay: Diagnosis and Significance of Minor Degrees of Uterine Abnormality in Relation to Pregnancy.

INSTITUTE OF CARDIOLOGY
5 P.M. (1, Wimpole Street, W.1.) Dr. Reginald Hudson: The Human Pacemaker and its Pathology. (St. Cyres lecture.)

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. C. H. Whittle: Ringworm from Animal Sources.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Mr. K. I. Nissen: Orthopædic Treatment of Various Neurogenic Conditions.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Small's Wynd, Dundee.) Sir Howard Florey: Some Properties of Endothelium.

Wednesday, 3rd

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.15 P.M. *History of Medicine.* Sir Weldon Dalrymple-Champneys: Wives of Some Famous Doctors. (Presidential address.)

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Prof. R. J. V. Pulvertaft: The Nature of Hodgkin's Disease.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. O. Oliver: Infective Agents in Skin Diseases.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. J. G. Scadding: Chronic Interstitial Fibrosis of the Lungs.

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (18, Nicolson Street, Edinburgh.) Dr. J. A. Strong: Relationship of the Endocrine System to Malignant Disease.

Thursday, 4th

ROYAL SOCIETY OF MEDICINE
5 P.M. *United Services.* Dr. E. M. Glaser: Treatment and Prevention of Motion Sickness.

POSTGRADUATE MEDICAL SCHOOL
4 P.M. Dr. R. I. S. Bayliss: Care of the Patient on Cortisone.

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Dr. A. Brodetti: Biomechanics of the Fractured Femoral Neck with Internal Fixation—an experimental study.

UNIVERSITY OF LIVERPOOL
5.15 P.M. (New Medical School, Ashton Street.) Prof. J. B. de C. M. Saunders (San Francisco): The Shoulder Joint and Its Dynamic Anatomy.

Friday, 5th

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. John Charnley: Treatment of Osteoarthritis of the Hip.

Notes and News

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

AT a meeting on May 21 Dr. IVAN POLUNIN, of the department of social medicine and public health, University of Malaya, read a paper on the Muruts of North Borneo and their declining population.[1] These indigenous inhabitants have, like the Red Indians of North America, the Aboriginals of Australia, and the Maoris of New Zealand, been diminishing in numbers for 30 years. This decline, Dr. Polunin had found, was due to a true excess of deaths over births and not to detribalisation, admixture with other races, or to emigration. The cause of the decline was obscure; epidemics of smallpox earlier in the century caused many deaths but no epidemics had occurred since the population began to decline, and on the positive side of the " balance sheet " headhunting had ceased. Malnutrition and endemic diseases, such as tuberculosis, but not malaria, had been excluded and it was concluded that the central problem was diminished fecundity of the Murut women. The recognised venereal diseases did not appear to be responsible for this, but examination of the vaginal flora of Murut women showed a high prevalence of anaerobic cocci of a type commonly associated with puerperal infections. The difficulties involved in carrying out a survey of the vaginal organisms in these women were very great: apparatus and culture media had to be taken into difficult territory, and cultures from the vagina had to be made and transported to Singapore, where they were freeze-dried and sent by air to Prof. Ronald Hare, of St. Thomas's Hospital, for detailed examination and typing. The difficulties were great, but still greater were those of persuading the Murut women to submit to vaginal examination. A high incidence of childless marriages was found among the Muruts and it was clearly hard to account for these on the basis of a puerperal infection. Inquiry, however, disclosed that abortion was commonly practised in nulliparous women, especially before marriage.

Professor HARE, opening the discussion, told how the bacteriological investigations in his laboratory had been done " blind ", and after having a considerable run of specimens nearly all of which contained anaerobic cocci, the next batches contained none. He suspected that something had gone wrong with the techniques involved, but careful check failed to reveal any faults in his laboratory. He raised the matter with Dr. Polunin and they both became very excited when they found that the negative specimens were all controls collected from women in a neighbouring tribe of high fecundity.

Dr. B. B. WADDY reported that similar depopulation was apparent in parts of northern Ghana. Epidemic diseases such as smallpox and meningococcal meningitis did not seem to be responsible, for their effects were temporary, but chronic endemic diseases such as trypanosomiasis and onchocerciasis were much more important. Dr. J. N. MCARTHUR considered that malaria might be an important factor in causing the Muruts' decline, for they lived in a highly endemic area and their neighbours did not. In view of the large number of childless marriages, Prof. H. E. SHORTT questioned the importance of postpartum infections as a cause of the decline.

Dr. POLUNIN, emphasising the complexity of the problem, said that if malaria caused depopulation it would do so by increasing infantile mortality and not by diminishing fecundity. Of the facts known the most important seemed to be that in Murut women infections of the reproductive tract with anaerobic cocci were common but were rare in neighbouring fecund tribes, and they were also rare in Great Britain. Other social research was necessary in order to explain the high incidence of childless marriages, but in this respect a lead lay in the finding that abortion was so common among these peoples that there was a higher incidence of genital abnormalities in non-parous women possibly caused by infection.

1. Polunin, I. *Lancet*, 1958, ii, 1005.

WORLD HEALTH ORGANISATION

THE financial committee of the Twelfth World Health Assembly, which is meeting in Geneva,[1] has recommended that W.H.O. should build a headquarters on a site to be given by the Canton of Geneva. The architect will be chosen by international competition, and the committee has accepted the offer of loans from the Swiss Confederation and Geneva totalling 30 million Swiss francs (£2½ million).

In a debate on malaria eradication, several delegates and Dr. M. G. Candau, the Director-General, pointed out that shortage of money would be the principal obstacle and that there might be a financial crisis in 1960.

Colombia and the Republic of Guinea have now joined W.H.O., which at present has 87 full members and 3 associate members.

TETANUS SPORES IN COTTON-WOOL

THE Ministry of Health has reminded hospitals that a survey [2] has shown that tetanus organisms may be present in unbleached cotton-wool (grey wool). Normally this would not be used for dressings, but it is sometimes used for padding splints, and may thus contaminate sterile dressings or actually infect wounds directly. Even bleached cotton-wool has been found in the past to contain tetanus spores, and the Ministry recommends that only cotton-wool known to be sterilised satisfactorily should be used for wound dressings.

BLINDNESS IN THE COMMONWEALTH

SURVEYS by the Royal Commonwealth Society for the Blind show an estimated 3 million blind in the Commonwealth, the society's report [3] states. Of these at least 50,000 are of school age, and over 2 million live in India, Pakistan, or Ceylon. The report recommends that the number of blind children at school should be increased from the present 1353 to at least 3000 in the next five years. In collaboration with the various missionary organisations this might be done by extending existing schools, establishing new ones, and enrolling blind children in ordinary schools; suggestions for training special teachers are also made.

The report emphasises that in the past there has been excessive preoccupation with the training of adults in urban areas only. If more than a small minority is to be helped some scheme for rural training and employment must be found.

At least two-thirds of blindness in the Commonwealth is preventable, and the society hopes to improve its facilities for research and treatment. In particular the possibility of controlling onchocerciasis in Ghana, developing a vaccine against trachoma, and providing a mobile treatment unit for conjunctivitis should be given priority. The problems of Asia, however, are so formidable that to be effective such programmes would have to be sponsored in collaboration with American, international, and other Commonwealth organisations.

RECORDS AND RECORDING

A PERIPATETIC correspondent [4] suggested the other day that efficiency does not always correlate with the elaborateness of the records department, and there may sometimes be a suspicion that people are making work for each other and recording useless data. A warning against this is one of many useful remarks in a Ministry of Health booklet.[5] This, the second of a series of pamphlets (the first was on outpatient waiting-time), deals in a cordial and down-to-earth way with a whole range of problems associated with the care of records and deployment of clerical and secretarial staff. The observations are based on a study of methods in 15 hospitals, 5 of which were teaching hospitals. Records should be organised by the lay administrators; and it is recommended that the

1. See *Lancet*, May 23, 1959, p. 1104.
2. Report of Public Health Laboratory Service. *Brit. med. J.* May 2, 1959, p. 1150.
3. The Next Five Years. Report of the Planning Committee of the Royal Commonwealth Society for the Blind, 121, Victoria Street, London, S.W.1. 1959. Pp. 18.
4. *Lancet*, May 2, 1959, p. 940.
5. Medical Records and Secretarial Services; Hospital O & M Service report no. 2; April, 1959. H.M. Stationery Office. Pp. 32. 2*s*.

records officer, in addition to securing liaison with the various departments, should address the relevant junior staff on the functioning of the system. The details of documentation, the use of colours, the costs of folders, printing, &c., and methods of storage are discussed at length. The Ministry does not seem very enthusiastic about microfilming techniques. There are some good points about tracing missing notes. One of the best sections is on the booking of outpatient appointments and on the conduct of the waiting-list.

As to the secretarial services, the booklet says that equipment for recording, by disc, cylinder, or tape, is essential for the best use of a typist's time; and the most satisfactory organisation is the central "pool" where each firm has its own secretary working under a supervisor, who can fill in gaps and deploy her staff to the best advantage.

The Ministry cannot be blamed for looking especially hard at the economic aspect, nor perhaps for its neglect of the research aspect: clearly institutions devoted in part to this end will wish to record many more data than those the Ministry seems to regard as adequate. They will also need an effective diagnostic index: this index is amazingly poor even in some of our most advanced hospitals, and the booklet gives some of the reasons.

To administrators this pamphlet is a "must"; but it would be good for consultants to skim through it, if only to learn that fancy case-note folders with pockets cost three and a half times as much as simple ones.

University of Cambridge

On May 16 the following degrees were conferred:

M.Chir.—J. T. Rowling.
M.B., B.Chir.—Sadrudin Alibhai Janmohamed (by proxy).
M.B.—A. J. R. Anderson, Jehangir Edalji Banatvala.

University of London

The following have passed the final examination for the degrees of M.B., B.S.:

Honours.—Ann D. Banister (*e*), University College; L. J. Beilin (*b*, *e*), King's College; J. S. Brown (*b*), King's College; J.S. Cameron (*c*, *e*), Guy's; Elizabeth H. Clapham (*a*), University College; Sylvia W. Davies (*a*), King's College; Julia P. Ellis (*a*, *c*), Middlesex; E. U. Essien (*c*), St. George's; Elizabeth A. Hills (*c*), St. Mary's; Shirley J. Knight (*b*), University College; Jean M. Kubale (*b*, *d*) Guy's; M. J. S. Langman (*e*), Guy's; N. J. Legg (*c*), St. Mary's; Ronald Marks (*c*), Guy's; R. E. May (*c*), Middlesex; T. J. Mott (*d*), Westminster; M. P. Vessey (*c*) University College; A. L. Whiteson (*c*), St. George's.

(*a*) *Distinguished in pathology;* (*b*) *distinguished in medicine;* (*c*) *distinguished in applied pharmacology and therapeutics;* (*d*) *distinguished in surgery;* (*e*) *distinguished in obstetrics and gynæcology.*

Pass.—S. O. Adenle, Margaret J. Alderton, Jennifer A. Allcock, A. E. E. Amua-Sekyi, M. G. Askew, Zahra Azari, K. T. Bailey, M. A. McL. Bailey, Katharine E. Barclay, E. J. Barnett, P. R. Barton, G. A. J. Beckley, A. D. Bell, H. C. Bentley, Arnon Bentovim, A. M. Birt, Balideo Bisseru, Ralph Blend, W. F. Bonner, Helen D. Bower, Pearl Bowman, Alice M. Bradley-Moore, J. L. Brady, J. K. Brennand, T. D. Brogan, P. L. Brooks, Dorothy A. Brown, Enid M. Brown, Doreen R. G. Browne, J. C. Bull, A. E. Bullock, D. I. G. Bunn, Jill A. Bunton, Ralph Burrows-Peakin, Hazel M. Burtenshaw, Christine M. Butler, J. R. Byles, B. G. D. Cameron, Dinah Castle, L. S. Castleden, R. H. C. Catty, P. C. S. Chapman, J. J. S. Chesser, D. D. Chundun, J. H. Cole, Daphne I. Cook, Edith M. Cooke, J. A. Corbett, Catherine M. M. Cordiner, A. M. Cotton, W. M. Cottrell, W. G. R. Couldrick, Felicity C. A. Cox, Jane M. Craig, B. E. Crawley, Barbara A. Croft, D. G. Davies, D. M. Davies, E. T. L. Davies, P. K. B. Davis, Peter Dewey, Harvey Dexter, Jack Diamond, G. H. Dickson, Judith Dimock, K. A. Doe, Geoffrey Douch, B. L. Dowling, M. S. Duffy, J. T. K. Duncan, Colin Dunstet, D. J. Y. Dyer, Margaret L. E. Eastcott, Susan C. Estcourt, B. A. Evans, D. S. Evans, Helen C. Evans, H. C. Evans, J. N. G. Evans, Jancis C. Evans-Prosser, Valerie J. Everett, Rosemary Fairweather, Monica J. Falkner, S. E. Farraj, M. A. Farrow, M. A. Fayyad, Elizabeth A. Featherby, L. H. Fenton, P. J. Fenton, Dorothy J. O. ffoulkes-Crabbe, Shirley Fish, Alexander Franklin, J. J. Franklin, Marie J. Freeman, M. C. Gabriel, Louise Gallagher, G. R. Gerson, A. D. Gibb, D. P. V. L. Giles, T. G. Gilfillan, E. W. Gillison, J. M. Glaisyer, Mervin Glasser, R. B. Godwin-Austen, Dulcie G. Gooding, P. G. Gooding, A. J. Gould, T. R. Gould, A. E. Green, R. S. Greenwood, Jane M. B. Griffiths, P. R. Grob, A. W. Grogono, D. R. Groves, Anne A. N. Grubb, R. H. Gwyn-Williams, Henry Haberfeld, Hanna F. Halaby, Katherine A. Hallidie-Smith, David Harding-Jones, C. E. Harley, J. A. Harper, John Harrower, B. A. Hasenson, T. H. Hayle, L. W. H. Hide, B. D. G. Hill, Elizabeth M. Hill, E. J. Holland, J. G. Holmes-Smith, William Holms, Joan M. Horder, Michael Horne, G. I. Horsfield, Judith A. Houghton, J. S. Howard, K. A. Howlett, K. N. Hudson, J. S. M. Hunt, Rosemary A. Hunt, M. F. Hyatt, Vivian C. Hyman, J. O. Ikpeme, D. C. Jeffery, Ann P. John, W. A. Johns, D. W. McN. Johnson, Michael Johnson, T. O. Johnson, A. F. Johnston, B. W. Jones, D. C. Jones, Shirley P. Jones, Younous Joomye, J. M. Justice, Arshalouis Kasbarian, J. B. Kelly, M. J. Kettle, R. L. King, A. F. I. D. Konoteye-Ahulu, P. J. Lacey, M. J. F. D. J. Lalouette, Gwenda D. Larkin, C. R. Lattimore, K. D. E. Lawrey, L. A. Lees, O. C. Legg, G. M. Levene, J. H. Lewis, Naomi U. Lewis, Diana J. M. Lister, T. A. Lloyd-James, V. J. E. D. Lobo, Cynthia Lucas, I. S. Macdonald, Peter McErlean, Hazel McFarlane, Anne M. Macgregor, C. G. McKenzie, Williamina T. A. McMath, K. S. A. Madgwick, J. J. Maher, Valerie Major, Sheila M. Malcolm, K. J. H. Mallett, K. C. Markwick, Helen K. Marston, J. L. Martin, D. D. Mathews, J. A. Mathias, R. W. May, Varazdad Melikian, D. J. O. Mills, H. J. Missen, J. D. Monger, John Monro, Margaret J. Moody, M. R. R. Moore, B. D. G. Morgan, Mary J. Morgan, Jean Morris, G. O. Morse, J. M. Motsieloa, J. C. Mountain, D. F. Munt, A. I. S. Murray, Mary A. Murray, Margaret L. Neale, Joan F. Nicholls, J. L. Nimmo, J. E. Noakes, R. G. Notley, E. L. Offerman, Barbara E. P. Ogden, Ruth Ogden, J. W. O'Higgins, E. E. Okafor, A. O. Olowu, D. J. Openshaw, E. H. Osborn-Smith, John Owens, H. L. Parfitt, Kathleen P. Parfitt, P. G. Parry, Adiline W. Patterson, M. J. Patterson, D. K. Payler, P. E. Pearce, W. B. Pearce, J. G. Pegg, D. G. Pendlebury, Audrey E. Pett, A. D. Piatkus, F. W. Pick, Jean S. Pilkington, Anthony Plews, R. C. H. Pollard, L. W. Purnell, R. J. Purnell, N. A. Purry, C. A. Ramsay, C. L. Ranasinghe, H. S. Rawdon Smith, D. C. Rawlins, M. I. Reeve, R. W. K. Reeves, P. R. Richards, A. H. Roberts, Jennie Robertson, A. N. M. Robinson, M. D. Robson, Peter Robson, B. K. Rogers, W. N. T. Roy, J. J. Russell, M. D. Sanders, Martin Sarner, D. A. Scarisbrick, J. G. Sekabunga, Anne Seymour, Margaret L. Shaw, H. D. Sherbourne, M. D. Sidell, P. H. Sills, M. O. Sime, R. B. D. Skidmore, Amy E. T. Smith, P. M. Smith, A. W. Sollom, R. W. Sparrow, A. J. Spicer, R. J. Spitzer, June M. Squire, Neilma J. Staunton, J. F. Steele-Perkins, Daphne J. Stevens, I. H. Stevenson, R. G. Swain, R. M. Swinburne, A. R. Tappin, Ann P. Taylor, Gordon Taylor, T. C. Taylor, A. J. Thomas, J. V. Thomas, W. K. Thomas, Pamela I. Tinslay, J. M. Tomlinson, Catherine R. Townsend, A. F. Tredre, Janet B. Tyler, M. J. Tyrrell, Joyce C. Vale, Athasit Vejjajiva, C. D. Walker, J. A. Wall, Rosemary V. H. Ward, Joyce Wardle, Margaret J. Watt, W. F. Webb, G. S. Welch, Mary K. West, Margaret J. Wharton, D. J. White, R. W. White, P. T. Whitehead, M. P. Wilderspin, M. C. T. Wilkes, M. K. Williams, B. C. Williamson, G. T. Wills, C. R. Wilks-Pepper, H. S. Winsey, J. Wolfle, M. J. F. Woolmore, D. S. Wright, R. J. Wrighton.

Royal College of Obstetricians and Gynæcologists

At the meeting of council on May 23, with Prof. A. M. Claye, the president, in the chair, the following were elected to council:

As representatives of the fellows: H. G. E. Arthure, William Hawksworth, H. J. Malkin, H. R. MacLennan, Ninian Falkiner.

As representatives of the members: Dorothy M. Shotton, M. M. Garrey.

Dr. T. F. Corkill (New Zealand) was appointed Sims-Black travelling professor for 1960.

The following were admitted to the fellowship:

B. H. Anderson, Segulla Jacob Aptekar, H. R. Arthur, Solomon Bender, B. E. Blair, Grace J. C. Browne, J. E. S. Carmichael, D. G. W. Clyne, J. B. Cochrane, S. J. Cohen, J. McD. Corston, Derk Crichton, G. L. Daly, Josephine A. Davidson, L. M. Edwards, H. H. Francis, I. T. Fraser, Sadashiv Narayan Gardé, Frans Gert Geldenhuys, B. W. Grieve, W. J. Hamilton, R. L. Hartley, J. R. E. James, W. F. Joynt, Jadwiga Karnicki, R. A. H. Kinch, Katharine I. Liebert, Ethna W. Little, J. L. Macarthur, J. M. McBride, Ian MacGillivray, J. S. MacVine, Agnes M. D. Milne, C. R. Morison, N. F. Morris, John Murray, Naizby Noble, Dwijendra Lal Poddar, L. J. Quinn, T. F. Redman, R. X. Sands, K. G. Seager, M. J. L. Stening, Elsie M. Terry, P. C. Thomas.

The following were admitted to the membership:

Ernest Aldous-Ball, K. R. Barnes, S. L. Barron, Kamala Bose, J. A. C. Brown, Enid M. Carey, Kalyani Chatterjee, Ki-Kit Chow, Sydney Cohen, K. V. Cooper, Mohini Dass, G. M. Davidson, B. H. Dawson, Suryamoni Devi, Rita D. Dickinson, Piyatissa Dissanayake, P. M. Elliott, R. G. Emerson, B. N. Foy, R. D. Fraser, Irene C. Hain, J. J. Handler, Shaukat Haroon, J. G. Harrington, Sakti Ram Hazra, Michael Howett, R. F. Hutchings, Sheila A. Martyn, Bimla Mehra, J. J. Morrissey, Harold Mukheiber, Saputahawattege Henry Piyadasa Nanayakkara, Ivan Orr, R. J. Ostolosky, J. F. O'Sullivan, Keki Dinshaw Printer, M. A. Pugh, Saroja Ramaswamy, Carmen M. Rant, Ann L. Reynolds, Jayatissa Nalin Rodrigo, Malti Rohatgi, Rita W. Shannon, D. H. Stewart, W. Siang Hwa Tow, Margaret A. Wignall.

The following have been awarded the D.OBST.:

P. J. Adams, K. D. Allardyce, C. J. Allen, D. L. Almond, Mary M. Anderson, P. C. W. Anderson, Antoni Zbigniew Andrzejowski, A. H. Atkinson, A. R. Archer, K. D. Austin, Sheila Baipai, Kenneth Barker, C. S. Barton, J. R. D. Bedford, Norman Beenstock, P. J. Bennison, J. A. Bessell, Anthea Blofeld, A. E. Bloomfield, A. R. Bone, G. A. W. Borland, T. A. Boxall, K. W. Braybon, D. S. C. Brown, E. W. J. Brown, Margaret Brown, J. R. Brunton, A. G. Bryer, J. G. S. Buchanan, Jill M. Buddin, G. D. Burnett, P. J. Burnett, B. H. Burns, Margaret E. Burns, J. L. H. Capper, R. P. Carrington, T. B. Catnach, Chandrabala Chaurasia, J. H. Chippendale, G. M. Clark, G. A. Clark, Gertrude A. Collie-Kolibabka, Jean R. Colston, S. J. Cooper, W. L. Cordeaux, A. W. M. Core, D. W. Couch, B. S. Cox, Frank Cramer, Douglas Cresswell, J. B. St. C. Cumberbatch, Peter Curzen, T. Ekundayo Dada, T. C. Dann, D. W. Davies, G. L. Davies, J. F. H. Deeble, B. P. Dillon, Kaushlya Dodeja, Margaret E. Dodson, G. V. Donaghy, I. E. Doney, E. M. Douglas, E. V. Dulson, Edna M. Dumbell, M. A. Edwards, Vivian G. Edwards, D. M. Entwistle, Elizabeth E. Evans, D. A. Ewing, G. R. Fenton, R. S. C. Fergusson, J. W. Fisher, C. V. Foll, R. D. Forbes, W. R. Forbes, J. M. Foster, J. G. Francis, C. R. Frazer, G. B. Gasson, L. J. German, S. D. Giddy, R. A. S. Gilchrist, L. H. Glaser, Norman Gorbutt, J. N. Graham-Evans, E. S. Grech, A. J. G. Griffin, M. T. F. Griffiths, Graham Gripton, Colin Gunn, C. R. Haines, J. G. Hall, J. M. Halpe, Ramsay Hannah, A. J. Harbott, John Hardy, Sylvie M. Harrison, M. W. Haslett, C. N. Haynes, Joyce R. Hayter, M. J. Hill, K. L. Hindle, M. N. Hirons, L. J. Hobbs, E. L. Holland, H. J. Houston, J. W. Gildas Hughes, J. H. C. Hunt, J. W. Hunt, Rosemary J. Huntley, G. D. Hurrell, R. C. Ilbert, Pilloo Khoodyar Irani, Hannah E. Jacoby, David Jarratt, M. C. Johnson, Barbara D. Jones, Kenneth Jones, Michael Kennedy, C. W. Kerr, P. N. Kersley, O. J. Kiener, J. I. King, Ma Hla Kyi, Khin Than Kywe, D. W. Laurie, M. H. Lawrence, Maimoon Mohamed Lebbe, J. W. S. Lee, J. V. V. Lewis, H. E. Lichtenstein, D. C. Linahan, Christobel H. Lomax, J. E. R. Lorimer, Elizabeth M. McM. Love, E. G. Lucas, W. L. MacIndoe, G. G. McGarry, Robert McLean, C. J. Macaulay, J. C. Mackenzie, I. W. Manson, Khursheed Homi Marolia, C. D. May, M. J. A. Menage, I. C. Menzies, J. D. Miller, W. R. Moore,

R. C. Mulholland, A. P. Murphy, Vidyasagar Nagpal, D. Y. Nelson, Grace E. Nicholls, A. M. Nisbet, C. H. Nourse, Florence Yokhaybaith Obadiah, F. T. O'Brien, Antoinette P. B. O'Donnell, B. K. O'Farrell, D. R. J. Parrott, D. W. Patient, Christine Pattie, Ethel Pereira, Paul Phellas, D. H. Pickett, F. J. Pickworth, J. S. Raban, J. L. Ramsay, G. A. Reed, J. M. Ritchie, Pamela A. Roberton, E. R. Roberts, James Roberts, M. R. G. Robinson, L. C. Rose, Ian Ross Russell, Gwyn Rowlands, Dilip Kumar Roy, C. S. K. Ruck, W. B. Russell, Kodathoore Shamba Shetty, J. A. Shanks, Michael Silver, M. N. Simmonds, M. W. J. Smith, R. D. Smith, J. G. Spink, G. P. St. C. Starck, R. H. Stearn, J. M. Steele, R. G. Strachan, C. D. Strang, D. R. M. Stuart, P. E. N. Suter, Seana R. Sutherland, G. B. Sutton, S. G. Sutton, H. M. Swallow, G. R. Swift, J. A. Taaffe, J. F. Taylor, S. A. W. Taylor, A. L. Thomas, K. T. Tighe, K. B Tyrer, Claudine M Tyson, R. M. Wainwright, A. K. Walker, J. G. Wall, Rosemary Wall, Barbara J. West, J. J. McL. West, M. S. Whitehouse, P. D. Wickenden, June M. Wilby, D. O. Williams, J. H. B. Williams, Meriel Williams, T. M. Winstanley, Raymond Winstone, J. F. Wood, A. K. Woodward, S. M. Worrall, M. J. Wright.

University of Birmingham

Dr. A. J. Essex-Cater has been given the title of part-time lecturer in child welfare in the department of pædiatrics and child health.

University of Edinburgh

Dr. G. R. Sutherland has been appointed assistant in the department of medicine, Dr. J. S. Robson senior lecturer in the department of therapeutics, and Dr. Viqar Zaman assistant in the department of zoology.

Royal College of Surgeons of England

Faculty of Dental Surgery.—On May 22 Lord Cohen of Birkenhead formally opened the new department of dental science, which has been set up by the Faculty to carry out research into the prevention of dental disease.

Faculty of Ophthalmologists

The following have been elected officers for 1959–60:

Mr. E. G. Mackie, president; Mr. J. E. M. Ayoub and Mr. G. W. Black, vice-presidents; Mr. G. T. W. Cashell, hon. treasurer; and Mr. E. F. King, hon. secretary.

Ciba Foundation

On Friday, June 26, at 5 P.M., at the Royal Institution, 21, Albemarle Street, London, W.1, Prof. Pasteur Vallery-Radot, of Paris, will give the Ciba Foundation lecture. He will speak in French and his subject will be Le Rôle de l'Intuition dans la Recherche Médicale. Tickets may be had from the assistant secretary of the Foundation, 41, Portland Place, W.1.

Society for Endocrinology

On Tuesday, June 23, at 5.30 P.M., at Burlington House, London, W.1, Prof. C. H. Best (Toronto) will give a lecture entitled A Canadian Trail of Medical Research.

British Pædiatric Association

Dr. E. W. Hart has succeeded Dr. P. R. Evans as honorary secretary of the Association. His address is the Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, London, W.C.1.

Association of Industrial Medical Officers

The annual provincial meeting of this Association will be held at Jordanhill Training College from July 13–17. Further particulars may be had from Dr. T. S. Wilson, 23, Montrose Street, Glasgow, C.1.

Israel Association of Chest Physicians

A convention on epidemiological problems of tuberculosis is to be held in Jerusalem on Sept. 22 and 23, after the International Tuberculosis Conference in Istanbul. Applications for registration for attendance should be sent to the Association, P.O. box 8123, Jaffo; and particulars about travel facilities may be had from Peltours, 28, Ahad Haam Street, Tel-Aviv.

Leeds Regional Hospital Board

Dr. A. A Driver has been appointed senior administrative medical officer to the Leeds Regional Hospital Board in succession to Dr. A. B. Williamson, who is retiring.

Dr. Driver qualified M.B. with honours at Leeds in 1937, and three years later he graduated M.D. Before his appointment in 1948 as assistant medical officer to the Leeds board he was successively medical superintendent of Seacroft Emergency Hospital and deputy medical superintendent of St. James's Hospital, Leeds. For the past five years he has been deputy S.A.M.O. to the Liverpool board.

Medical Association for the Prevention of War

This association will hold a symposium on the causes of war on Saturday, June 6, at 2.30 P.M., at Kingsway Hall, London, W.C.2. The speakers will be Prof. T. H. Pear and Dr. Lucy Mair. The discussion will be opened by Dr. Alex Comfort.

International Conference on Medical Electronics

This conference will be held in Paris from June 24 to 27. The deputy secretary is G. Verdeaux, 63, Boulevard Saint-Michel, Paris 5e.

Czechoslovak Society of Gastroenterology and Nutrition

This society is to hold a congress from Sept. 21 to 24 in Carlsbad. Further particulars may be had from Dr. J. Mašek, Nutrition Research Institute, Budějovická 800, Prague 14-Krč.

International Congress of the Medical Press

This congress will be held in Cologne from July 3 to 6. The programme will include a discussion on the medical organisation as a publishing firm which will be opened by Dr. H. A. Clegg. Further particulars may be had from Dr. F. Oeter, Köln-Lindenthal, Haedenkampstr. 1 (Bundesärztehaus).

Prof. Robert Platt, P.R.C.P., has been elected an honorary member of the Association of American Physicians.

Mr. M. C. Wilkinson, orthopædic surgeon at Black Notley Hospital, Braintree, Essex, is visiting Poland from May 27 to June 3, under the auspices of the British Council. Mr. Thomas Menzies will visit Warsaw for a week in July to give surgical lectures.

Semipermanent exhibitions are available during the summer course at the Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, London, W.C.2. The second, from June 3 to 30, by Dr. R. G. Cochrane, will be on Leprosy.

The cricket match between the B.M.A. and the Law Society at Hurlingham on May 24 was drawn: B.M.A. 249 for 5 dec., Law Society 192 for 8. For the B.M.A., A. P. H. Wilkinson (108) and I. A. H. Munro (66) scored 177 for the first wicket, G. Barwell made 34, and C. B. Clarke took 6 for 57.

CORRIGENDUM: *The Drug Bill.*—In our leader of May 16 we said that neither the Hinchliffe nor Douglas reports mentioned a card index as a means of supplying information to doctors. In fact the Hinchliffe Committee said that they did not regard a card index, with the extra clerical work it would entail, as a practical source of reference for the busy doctor.

Appointments

DEANS, MADELINE, M.B. Aberd., D.P.H.: assistant M.O., Inverness County Council.
GREEN, R. A., M.B. Cantab., F.F.A.R.C.S., D.A.: consultant anæsthetist, St. George's Hospital, London.
EVANS, R. G., M.B., B.SC. Wales, D.P.H.: M.O.H. and principal school M.O., Breconshire.
HOLT, P. G., M.B. Lpool, D.P.H.: district M.O.H., Cromer, Sheringham, and Erpingham.
MOORE, F. H., M.B. Dubl., F.R.C.S.E.: assistant orthopædic surgeon, Law Hospital, Carluke, Lanarkshire.
PEEBLES, DALZIEL, L.R.C.P.E.: administrative M.O., Western Regional Hospital Board, with whole-time duties at Falkirk and district hospitals.
SCHOFIELD, SHEILA F., M.B. Leeds, D.C.H., D.P.H.: senior assistant M.O. and school M.O., Harrogate, Knaresborough, and Nidderdale.

Colonial Appointments:

AWOLIYI, ELIZABETH A., M.R.C.P., D.C.H., D.OBST.: specialist (gynæcologist), Nigeria.
BARRY, N. A., L.R.C.P.I.: M.O., Uganda.
BRICE-SMITH, JOHN, M.R.C.S.: M.O., Uganda.
CONACHER, D. G., M.B. Edin., D.T.M. & H., D.P.H.: senior M.O., Tanganyika.
DE WRIGHT, F. G. L., M.B.: M.O., Uganda.
DOS SANTOS, W. A., M.B. Cantab., DIP. BACT.: senior specialist (pathologist), Nigeria.
GRIFFITH, G. V. A., M.D. Dubl.: D.M.S., British Honduras.
LAKEMAN, MARGARET A., M.B. Lond., M.R.C.O.G.: specialist (gynæcologist), Eastern Region Nigeria.
MOORE, S. H., M.B., B.SC. Dubl., D.P.H.: assistant director of health services, medical department, Hong Kong.
NICHOLSON, J. A. B., M.B.E., M.B. Lpool, D.P.H.: D.D.M.S., North Borneo.
RAYMAN, M. R., M.B. Lpool, F.R.C.S.: surgeon, British Guiana.
RUTLEDGE, GEORGE, M.B. Belf., F.R.F.P.S., D.C.H.: M.O. (special grade), Uganda.
TEELOCK, BOODHUN, M.B. Edin., D.T.M. & H.: senior schools M.O., Mauritius.
TENG, PIN HUI, M.B. Hong Kong, D.P.H.: A.D.M.S., medical department, Hong Kong.